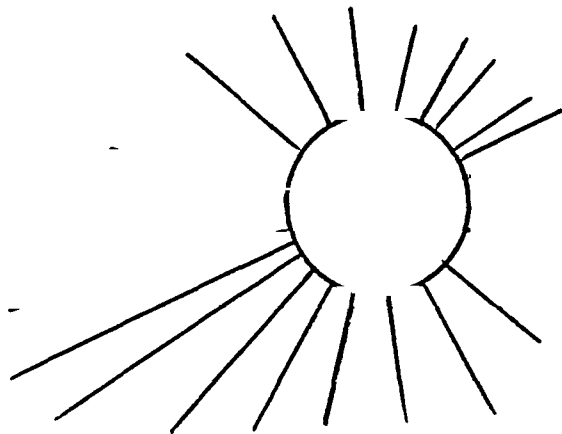


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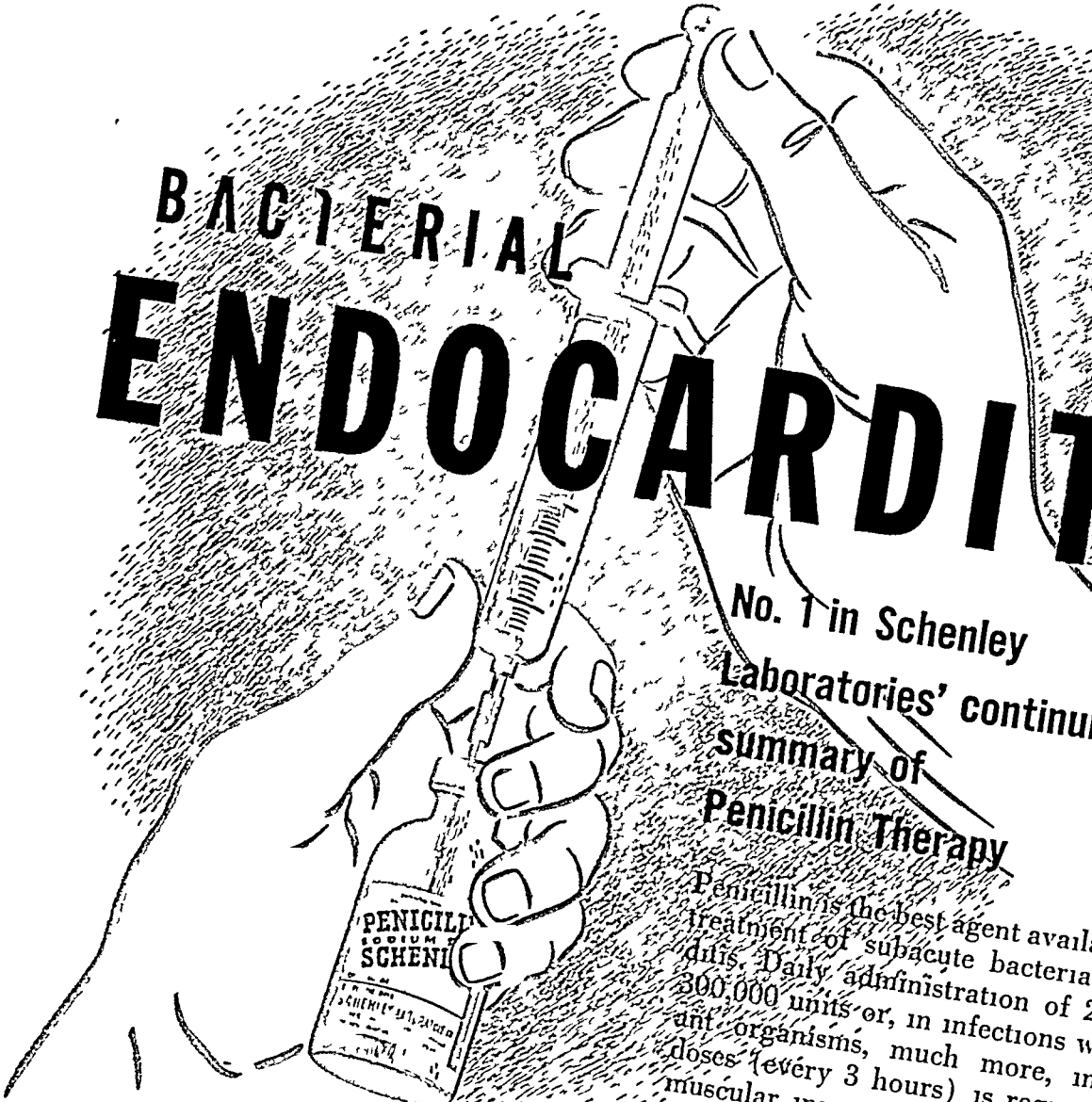
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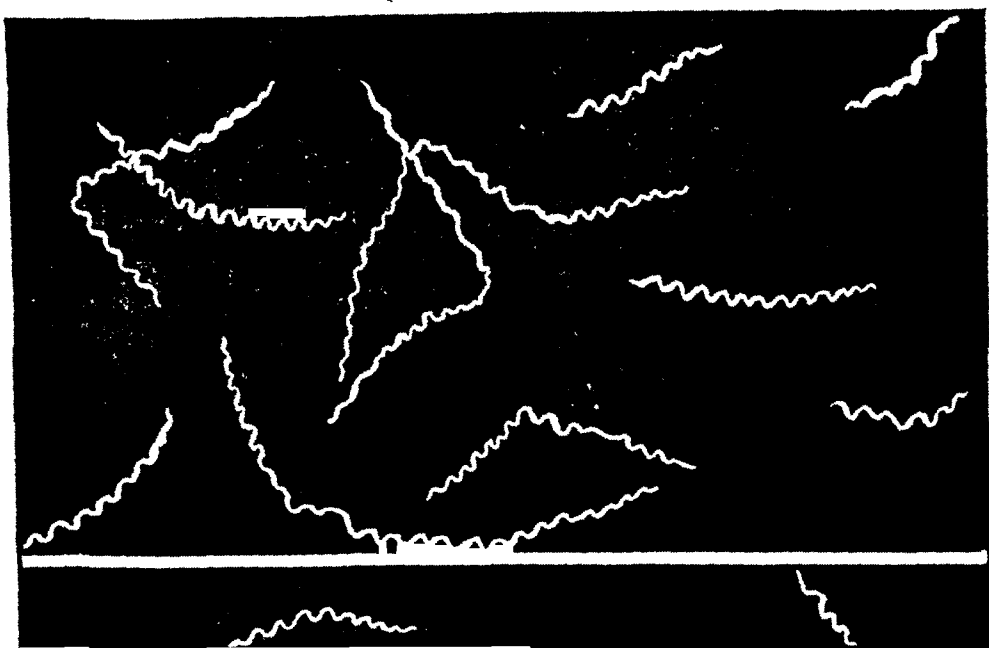
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<sup>1</sup>U.S. Nav. M. Bull. 45:783, 1945, and previous annual Navy reports

<sup>2</sup>Stokes, J. H., Beerman, H. and Ingraham, N. R.: *Modern Clinical Syphilology*, ed. 3, Philadelphia, W. B. Saunders Company, 1945, pp. 359, 300



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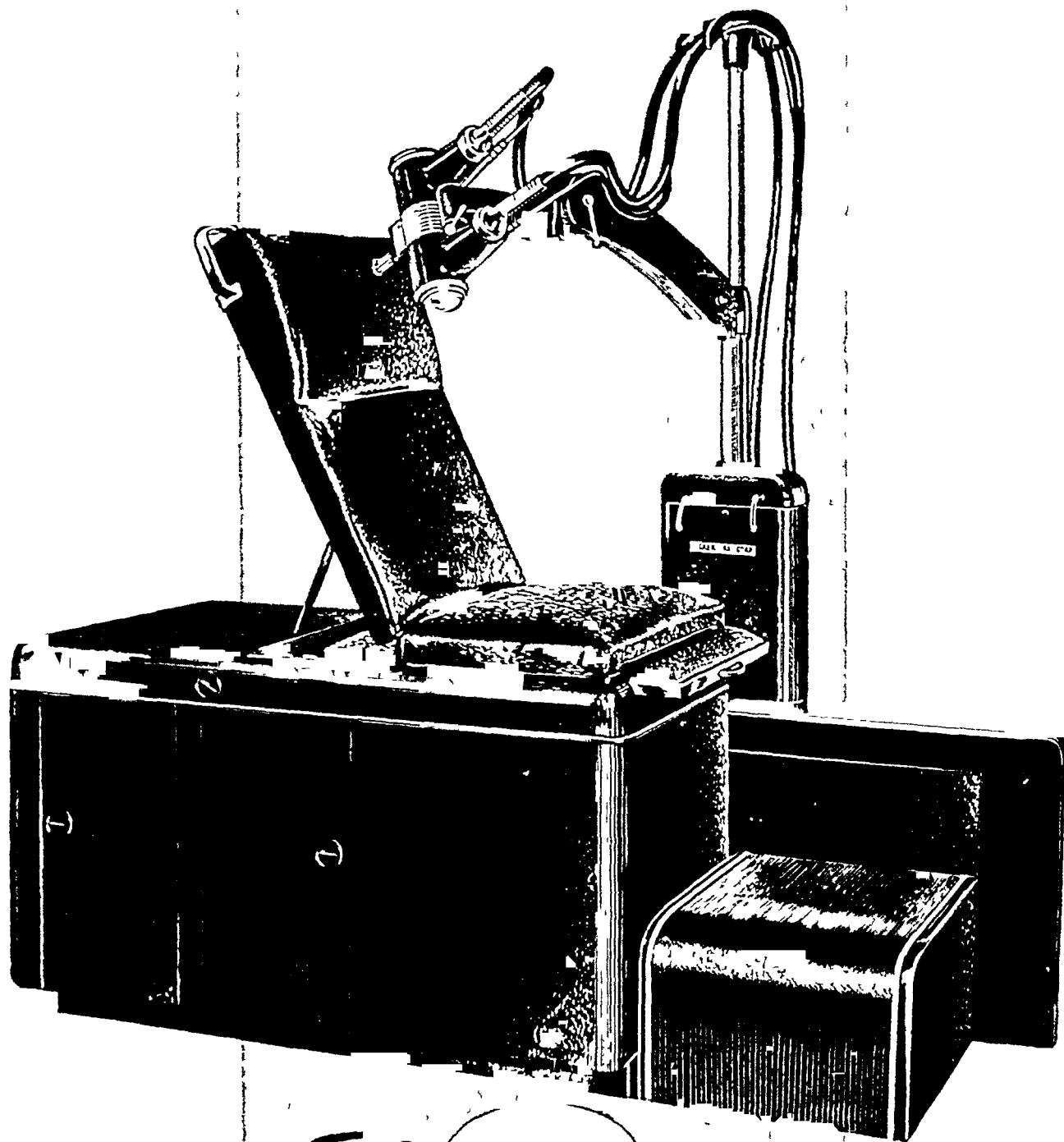
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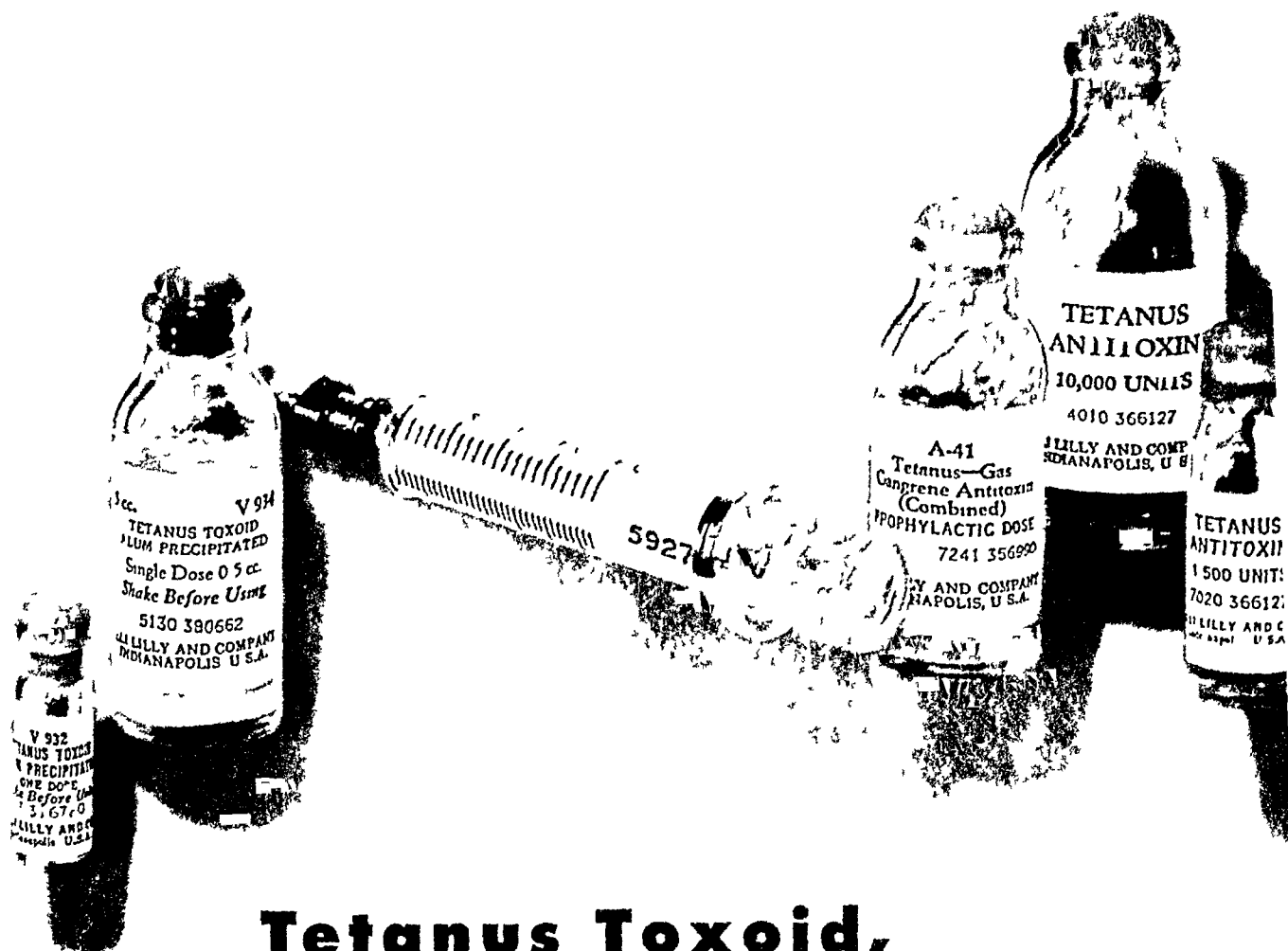
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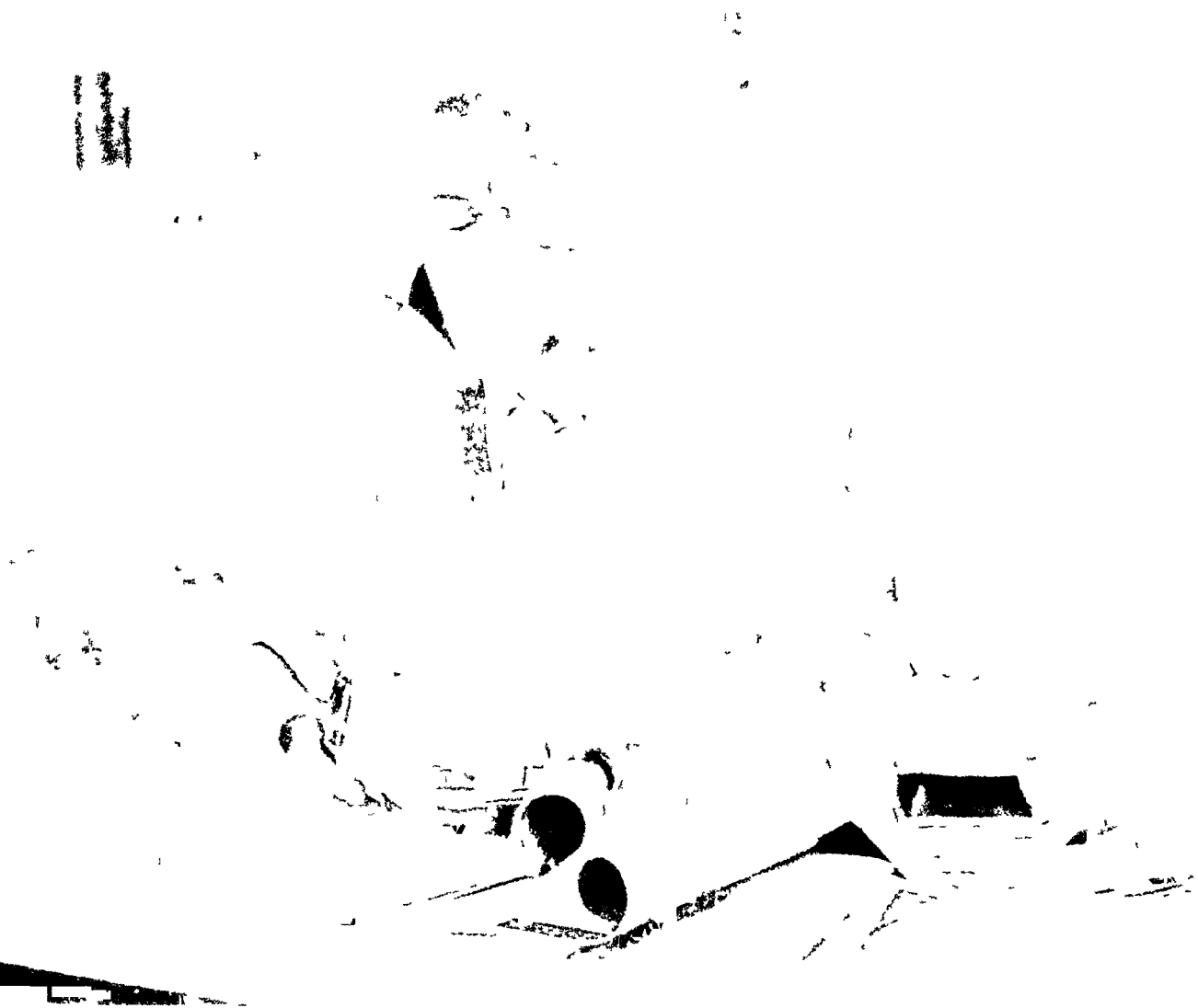
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There is little rest for the busy physician even after the responsibilities to his patients have been satisfactorily discharged. Medical journals subsist entirely on the writings of physicians. The articles, designed for the purpose of sharing knowledge with others, require arduous toil, and time not available during office hours. It is well to remember then, in reading medical journal papers, that some physician somewhere may have worked far into the night with the hope that his colleagues would benefit.

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# Archives of Dermatology and Syphilology

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## LATENT SYPHILIS

Study of One Hundred and Sixty-Nine Cases Observed Ten Years or More

JAMES W JORDON, M D

AND

FRANK A DOLCE, M D

BUFFALO

ONLY meager information on the outcome of treated and untreated latent syphilis is available in the literature. The reason for this is that no information of value can be obtained except by follow-up studies of patients observed over a period of many years. It is our opinion that at least ten years, and preferably a lifetime, must intervene from the time of the first observation of the patient before any attempt can be made to evaluate the efficacy of treatment rendered or to determine the outcome of untreated syphilis. Furthermore, only by observation of such patients over a period of many years can data be obtained as to the proper amount of treatment that patients with latent syphilis should receive to prevent complications in later life and to determine what relation, if any, serologic tests have on the final clinical outcome. Most texts on syphilology cite the figures compiled by the Cooperative Clinic Group in 1932<sup>1</sup> on the outcome of treated latent syphilis and those gathered by Bruusgaard in 1929<sup>2</sup> on the prognosis of untreated syphilis. The comprehensive work done by the Cooperative Clinic Group in regard to treated latent syphilis enumerates results of observations on only 40 patients followed ten years or more, and, although in this report data are presented on many hundreds of treated patients with latent syphilis, it is our opinion that figures for those followed less than ten years are of little or no value in determining the effectiveness of treatment in preventing late complications.

Read at the Sixty-Fifth Annual Meeting of the American Dermatological Association, Inc., Chicago, June 20, 1944

From the department of Dermatology and Syphilology of the Edward J Meyer Memorial and the Buffalo General Hospitals and the University of Buffalo School of Medicine

1 Moore, J E, and others. Cooperative Clinical Studies in Treatment of Syphilis, *Ven Dis Inform* **13** 371 (Oct 20) 1932

2 Bruusgaard, E. Ueber das Schicksal der nicht spezifisch behandelten Luetiker, *Arch f Dermat u Syph* **157** 309, 1929

Recently Kahn and Becker<sup>3</sup> published a paper on the results of the treatment of 200 persons with latent syphilis with relatively large amounts of bismuth but most of their patients were followed for only short periods and accordingly little is known about the ultimate clinical outcome of this group of patients since they were not observed for a sufficiently long period. Also Discker, Clark and Moore<sup>4</sup> reported on the clinical outcome of 926 cases of latent syphilis observed five years or more and emphasized that the serologic outcome was unimportant and unrelated to the clinical outcome. The authors expressed the belief that the optimum amount of treatment for latent syphilis is approximately twenty injections of an arsenical and a corresponding number of injections of a heavy metal, regardless of the state of the blood serum at the time of cessation of treatment.

Not only is there slight information available on the ultimate clinical outcome in cases of treated latent syphilis but there is likewise little information on the ultimate outcome in cases of untreated syphilis. Data on this subject are difficult to compile since again only observation of untreated patients over a period of many years can throw any light on this subject. The only data of any importance gathered on this subject are those compiled by Bruusgaard, who observed 309 patients with untreated early syphilis from three to forty years after the infection and reported that about 28 per cent had negative Wassermann reactions and approximately 28 per cent had either a positive serologic reaction or benign late syphilis. While the data compiled by Bruusgaard are the most valuable thus far collected on the outcome of untreated early syphilis they by no means furnish complete information, since most of his patients did not have repeated serologic tests, and it is our opinion that only repeated serologic examinations over a period of many years can furnish conclusive information on the question of spontaneous serologic cure. Also the group of patients with whom he started had frank early syphilis for whom, some observers believe, there is a more favorable prognosis than for persons in whom no clinical manifestations of early syphilis occur. The latter type of patients were not considered in his report nor was he able to include Negroes in his study. Because of this necessary omission on Bruusgaard's part his figures do not truly represent the facts for a mixed white and Negro population since it is well known that the percentage of late cardiovascular syphilis is much higher in the Negro race.

<sup>3</sup> Kahn, D. and Becker, S. W. Use of Bismuth Compounds in Syphilotherapy. Results of Treatment of Latent Syphilis by Bismuth Compounds Combined in Part with Arsenicals. *J. A. M. A.* **120**: 338 (Oct. 3) 1942.

<sup>4</sup> Discker, T. H., Clark, E. G. and Moore, I. F. Long-Term Results in the Treatment of Latent Syphilis. *Am. J. Syph., Gonorr. & Ven. Dis.* **28**: 1 (Jan.) 1944.

Our study presents data obtained on 169 patients with latent syphilis observed ten years or more, 100 of whom were considered well treated and 69 poorly treated. The Meyer Memorial Hospital clinic, from which most of the data have been obtained, is a large hospital which takes care of the medical and dental needs of a high percentage of the indigent people of the city. It furnishes hospitalization, outpatient clinic service and home call service and has numerous dispensaries throughout the city. Because of these services many patients report back to the hospital at frequent intervals, and, because of this, patients with syphilis are observed over a period of many years. This results in repeated physical examinations and serologic tests.

The term "latent syphilis" as employed in this study means that there were no clinical signs and symptoms of syphilis at the time of the examination of the patients. Diagnosis was usually made because of repeatedly positive serologic reactions or the birth of a congenitally syphilitic child. Examinations of the spinal fluid were made at least once for 94 of the 100 patients in the well treated group and for 29 of the 69 patients in the poorly treated group. No patient known to have had a positive spinal fluid on the first examination is included in this study, and no patient who did not have a spinal fluid examination and in whom later a syphilitic neurologic complication developed is included. These, plus an observation period of ten years or more, were the only criteria for the selection of patients. The period of ten years was decided on because it was our opinion that in a syphilitic person without clinical evidence of the disease serious complications require several years to develop and that death from such complications in less than ten years is a remote possibility.

The serologic tests made at the first examination of the patients were the standard New York state Wassermann test then in vogue and the standard Kahn test. Subsequent serologic tests also were standard New York state Wassermann and Kahn tests, with refinements as they developed. The tests therefore at the end of the period of observation may, in general, be said to be more sensitive than those employed at the time of the original diagnosis.

The 169 patients were divided into two groups solely on the basis of the total amount of treatment received. Group I, considered poorly treated, consisted of 69 patients who received either no treatment or less than a total of forty injections, and group II, considered well treated, consisted of 100 patients who received forty or more injections of an arsenical drug and a heavy metal, either alone or in combination. In most instances the arsenical drug employed was arsphenamine, the average dose 0.3 to 0.4 Gm. On some occasions neoarsphenamine, silver arsphenamine or sulfarsphenamine was employed. None of the patients was treated with oxophenarsine hydrochloride, since this drug

serious late syphilitic heart disease had developed. In addition to the cardiovascular complications, two more certain complications developed, in 1 patient <sup>5</sup> paresis developed and in another a late cutaneous syphilid. In another patient hepatic cirrhosis developed probably unrelated to the syphilitic infection.

Our patients showed a high incidence of cardiovascular complications. It is our opinion that this does not reflect the general trend of untreated latent syphilis observed over an average period of thirteen years. We felt that some of the 12 patients with aortic insufficiency and saccular aneurysm returned to the hospital as a result of symptoms coincident with these complications and therefore not all can be included in an estimation of the percentage of untreated latent syphilitic patients in whom cardiovascular syphilis will develop. We do believe, however, that the 13 patients with aortitis confirmed by roentgenologic

TABLE 2—*Complications of Latent Syphilis Poorly Treated*

	Number	Per Cent
1 Cardiovascular		
Probable aortitis (physical signs)	4	
Aortitis roentgenologically confirmed	13	
Aneurysm	5	
Aortic insufficiency	6	
Aneurysm and aortic insufficiency	1	
Certain cardiovascular complications	25	36.2
Probable	29	42.0
2 Other complications		
Paresis	1	
Hepatic cirrhosis	1	
Late cutaneous syphiloid	1	
	3	
Total certain complications	27	39.2
Total probable complications	32	46.3

examination and the 4 with probable aortitis did not return to the hospital as a result of this complication, since in most instances the aortitis was discovered on routine physical and roentgenologic examinations and symptoms were minimal.

From our observations, we believe that in 20 to 25 per cent of persons with untreated or poorly treated latent syphilis some cardiovascular complication will develop in later life. This figure is approximately twice that estimated by Moore, based on Bruusgaard's data, but one must remember that Bruusgaard's patients were all white, that many had not reached the age when cardiovascular complications develop, and that all had frank early syphilis. On the other hand, our group includes 39 Negro patients among whom cardiovascular com-

5 This patient had negative clinical signs and symptoms of syphilis and a negative spinal fluid when first observed. Fourteen years later, when paresis developed the spinal fluid was strongly positive.

plications are expected to be much higher. Most patients had reached the age when cardiovascular complications develop, and the study includes patients who did not have frank early syphilis.

*Relationship of the Serologic Reaction of the Blood to the Development of Complications* Of the 16 patients who had negative serologic reactions of the blood during the last four years or more of observation none had certain but 3 had probable late complications. These were suspected of having aortitis. In the 24 patients whose reactions varied from negative to positive but were not negative during the last four years or more of observation, 2 certain cardiovascular complications and 1 probable one developed. The cases of paresis and hepatic cirrhosis occurred in this group. The 29 patients whose blood serum was fully positive on all occasions when it was examined had twenty-three certain cardiovascular complications. The case of tertiary syphilis of the skin also occurred in this group (table 3). This fact suggests that consistently

TABLE 3—*Relationship of Serologic Reaction of the Blood to Development of Complications in the Poorly Treated Group*

Serologic Reactions	Cases, No	Complications			
		Certain, No	Probable, No	Certain, per Cent	Probable, per Cent
Negative last 4 years or more	16	0	3	0	18.7
Less than maximum positivity on one or more examinations but not negative last 4 years	24	3	2	12.5	8.3
Consistently fully positive	29	24	0	82.7	0
Totals	69	27	5		

positive blood serums in poorly treated syphilitic patients observed over a considerable period is a bad prognostic sign, and, likewise, fluctuation in or reversal to negativity of the blood serum is a good prognostic sign. Therefore, if syphilis is present in patients with doubtful serologic reactions the ultimate clinical outlook may be good even if treatment is withheld.

Physicians frequently see patients who have weakly positive or doubtful serologic reactions and are in a dilemma as to whether the patient has syphilis. They are fearful that if syphilis is present they may do harm by withholding treatment and that if syphilis is not present they may cause unjustifiable mental anguish and physical discomfort and subject the patient to the risk of a major reaction if treatment is instituted. Our studies suggest that little or no harm will result from withholding treatment in such cases, and it is our belief that treatment should not be administered when there is no other evidence of syphilis, including history, than weakly positive serologic reactions, except possibly for pregnant women.



*Relationship of Frank Early Syphilis to Late Complications*—Eighteen of the 69 patients gave a history suggestive of primary or secondary syphilis and in this group there were 8 with certain cardiovascular syphilis and 2 with probable cardiovascular syphilis. There was also 1 with tertiary syphilid of the skin, and the patient with paresis belonged in this group (table 4). This brings up the question whether an early well marked tissue reaction to the spirochete is evidence of immunity on the part of the host or whether such a strong tissue reaction indicates a greater degree of allergy to the spirochete, and therefore an increased tendency toward development of late serious complications of syphilis. Of the total certain late complications, ten of the twenty-seven occurred in this group of patients, an incidence

TABLE 4—*Relationship of Frank Early Syphilis to Late Complications in Poorly Treated Patients with Latent Syphilis*

		Complications, per Cent	
Number giving history	18		
Males	15		
Complications			
Certain cardiovascular	8	53.3	
Probable cardiovascular	2	13.3	
Total	10	66.6	
Females	3		
Complications			
Tertiary cutaneous syphilid	1	33.3	
Paresis	1	33.3	
Total	2	66.6	
Total number certain and with probable complications	12	66.6	

of 55.5 per cent, while for the entire group the incidence of certain complications was 39.2 per cent. It appears therefore that patients with frank early syphilis have a prognostic outlook no better than, if as good as, those in whom early symptoms are minimal or absent.

#### DATA ON GROUP II

Of the 100 patients who received more than a total of forty anti-syphilitic injections, there were 52 men and 48 women. Of these, 37 were white men, 15 Negro males, 35 white women and 13 Negro women. The average age of the patients when first examined was 37.1 years. They were observed over an average period of eleven and three-tenths years, therefore the average age at the end of the observation period was 48.4 years. The longest period of observation was nineteen years, and 9 of the patients were observed fifteen years or more. Thirty of the 100 gave a history of early syphilis. This group had had syphilis an average of eleven and seven-tenths years.

The patients received an average of twenty-eight and seven tenths injections of an arsenical drug and seventy-eight injections of a heavy metal

*Serologic Reactions of the Blood During the Period of Observation*

—Of the serologic reactions determined prior to treatment, 78 were of maximum positivity, 11 were moderately positive and 11 were weakly positive. During the period of treatment and observation, 9 patients had fully positive reactions on all subsequent examinations, 12 had reactions varying from strongly positive to completely negative and 5 from weakly positive to strongly positive, 12 had reactions which remained weakly positive and were at no time completely negative, the reactions of 22 varied from weakly positive to entirely negative, and 40 had negative serologic reactions for the last four or more years of observation. Seventy-four of the 100 patients had negative serologic

Table 5—*Serologic Reactions of the Blood of Well Treated Patients with Latent Syphilis*

Prior to treatment	
Maximum positivity	78
Moderately positive	11
Weakly positive	11
Total	100
During the observation period *	
Consistently strong	9
Strong to negative	12
Weak to strong	5
Weak	12
Weak to negative	22
Negative last four years or more	40
Total	100

\* Seventy-four patients had negative serologic reactions sometime during observation, while 91 had a tendency toward reversal (that is, less than maximum positivity) several times during observation.

reactions at some time or other, but the reactions of only 40 of the 100 remained negative four years or more. Sixty-nine of the 78 patients who had fully positive reactions on the first examination showed a tendency to serologic reversal, that is, the reaction was not fully positive several times during the period of observation (table 5). It is obvious from this fact, as in the cases of poorly treated patients with latent syphilis, that one must be guarded in speaking of serologic cure, since there is a decided tendency for the blood serum of patients with treated latent syphilis to fluctuate over a period of years. The serologic reaction may be entirely negative at one time and may range from weakly to strongly positive at another. We did not believe that even the group that had negative reactions four years or more could be regarded as serologically cured. Longer observation or more frequent serologic tests might have shown variation in their reactions. Only

17 per cent more of the well treated patients had negative serologic reactions during the last four years or more of observation than of the poorly treated patients, therefore, antisyphilitic treatment of latent syphilis as administered by us resulted in only a 17 per cent doubtful increase in the number of serologic cures above that spontaneously achieved in the poorly treated group. The Cooperative Clinic Group reported that from the standpoint of serologic reactions 85 per cent of their 40 patients followed ten years were cured, however, if repeated negative reactions over a period of years had been their criterion for serologic cure it is doubtful that their percentage would be nearly so high. If serologic cure is the objective in the treatment of latent syphilis, it is obvious from our figures that our treatment was a failure.

*Complications Which Developed in the Well Treated Group*—In the 100 well treated patients, four complications developed. Two of these were aortitis confirmed by roentgenologic examination, and two others were cases of saccular aneurysm. There were no other complications.

TABLE 6—*Relationship of Serologic Reactions of the Blood to Complications in Well Treated Patients with Latent Syphilis*

Complication	Number of Cases	Serologic Reactions of Blood
Aortitis	1	Weak to positive 5 yr prior to onset
Aortitis	1	Negative 3 yr prior to onset
Saccular aneurysm	1	Negative 9 yr prior to onset
Saccular aneurysm	1	Varied moderately from positive to negative

Thus treatment of this group resulted in an incidence of late complications of 4 per cent, as compared with 39 per cent in the poorly treated group, and while a failure from the serologic standpoint, the treatment was brilliantly successful from a clinical point of view.

*Relationship of Serologic Reactions to Complications in Well Treated Group*—Of the 2 patients with aortitis, 1 showed a variation in serum from weakly positive to negative for five years prior to the onset of clinically recognizable aortitis. In the other, the blood serum was negative for three years prior to the onset. In 1 patient in whom an aortic aneurysm developed, serologic reactions had been negative for nine years prior to the development of aneurysm, and in the other the reactions varied from moderately positive to negative (table 6). Thus, it is obvious that in the case of well treated latent syphilis, the condition of the blood serum bears no relationship to the development of complications, inasmuch as all patients in whom complications developed showed a decided tendency to serologic reversal. It is our opinion, therefore, that serologic reactions in well treated patients with latent syphilis are of no prognostic importance and cannot be used as a guide to treatment. We therefore agree with Discker<sup>4</sup> and his co-workers that too much emphasis has

been put on the serologic cure of patients with latent syphilis while the only important consideration is the prevention of late complications. There is, in our opinion, no connection between these two factors. Patients in whom the blood serum fails to become negative with treatment do at least as well from a clinical standpoint as do those whose serum becomes negative.

*Relationship of Clinical and Serologic Outcome to Amount of Treatment Given in the Well Treated Group* The well treated patients were divided into subgroups based on the number of injections of an arsenical drug and also on the number of injections of a heavy metal they received. The clinical and serologic outcome of these subgroups was compared. Based on the number of injections of an arsenical drug, the patients were divided into three subgroups (table 7). The first of these subgroups received nineteen or less injections, the second twenty to twenty-nine

TABLE 7—Summary of Results According to Amount of Treatment with an Arsenical in Well Treated Patients with Latent Syphilis

Number of Injections	Number of Cases	Serologic Reactions of Blood During Observation		Complication		
			No	%	No	%
0-19	22	{ Negative 4 yr. or more	7	31.8	Aortitis	2
		{ Varied	12	54.5	Aneurysm	1
		{ Strongly positive	3	13.6		
20-29	24	{ Negative 4 yr. or more	12	50.0	0	0
		{ Varied	11	45.8		
		{ Strongly positive	1	4.1		
30 or more	54	{ Negative 4 yr. or more	21	38.8	Aneurysm	1
		{ Varied	28	51.8		
		{ Strongly positive	5	9.2		

injections, and the third, thirty or more injections. In the first subgroup there were 22 patients. Seven, or 31.8 per cent, of these had a negative blood serum during the last four or more years of observation. In this subgroup three or four complications occurred, in 2 patients a syphilitic aortitis developed and in 1 an aneurysm of the aorta, making the percentage of complications in the group 13.6 per cent. Twenty-four patients received twenty to twenty-nine injections. Twelve, or 50 per cent, of this subgroup had negative serologic reactions during the last four or more years of observation, and there were no complications. Fifty-four patients received thirty or more injections. Twenty-one, or 38.8 per cent, of this subgroup had negative serologic reactions during the last four or more years of observation, and 1 patient in this group acquired an aneurysm of the aorta.

The data show that there is only slight gain from a serologic standpoint if large amounts of arsenical drugs are used. In the group which received nineteen or less injections, 31.8 per cent had negative serologic reactions during the last four or more years of observation. In the group

which received twenty to twenty-nine injections of an arsenical drug, the percentage rose to 50, but in the group which received thirty or more injections the percentage again fell to 38.8. From a serologic standpoint, twenty to twenty-nine injections of an arsenical drug produced the best result, further arsenical therapy accomplished nothing from this standpoint. From the clinical standpoint, the poorest results were obtained in the group which received nineteen injections or less of an arsenical drug and in whom three of the four complications developed. There were no complications in the group which received twenty to twenty-nine injections of an arsenical drug, but in 1 patient in the group which received thirty or more injections aneurysm developed. Thus, from a clinical standpoint twenty to twenty-nine injections of an arsenical drug also produced the best result, while further arsenical

TABLE 8—*Summary of Results According to Amount of Treatment with a Heavy Metal in Well Treated Patients with Latent Syphilis*

Number of Injections	Number of Cases	Serologic Reactions of Blood During Observation		Complication		
			No	%	No	%
40-69	14	{ Negative 4 yr. or more	6	42.8	Aneurysm	1
		{ Varied	5	35.7		
		{ Strongly positive	3	21.4		
70-99	33	{ Negative 4 yr. or more	14	42.4	Aortitis	1
		{ Varied	18	54.5		
		{ Strongly positive	1	3.0	Aneurysm	1
100-139	32	{ Negative 4 yr. or more	15	46.8	Aortitis	1
		{ Varied	14	43.7		
		{ Strongly positive	3	9.5		
140 or more	21	{ Negative 4 yr. or more	5	23.8	0	0
		{ Varied	14	66.6		
		{ Strongly positive	2	9.5		

therapy failed to prevent the development of aneurysm in 1 case. Of the 78 patients in the second and third subgroups who received twenty or more injections of an arsenical drug, there was only 1 late serious complication—an incidence of 1.3 per cent.

The clinical and serologic results obtained by varying numbers of injections of a heavy metal were compared in the same way as were the results with arsenical drugs (table 8). The 100 patients were divided into four subgroups. The first of these subgroups, comprising 14 patients, received between forty and sixty-nine injections, 6 of these patients (42.8 per cent) had negative serologic reactions during the last four or more years of observation. One aneurysm of the aorta occurred in the group. There were 33 patients in the second subgroup, they received between seventy and ninety-nine injections. Fourteen or 42.4 per cent, of these patients had negative serologic reactions during the last four or more years of observation. There was 1 case of aortitis and 1 of aneurysm. In the third subgroup there were 32 patients, they

received between one hundred and one hundred and thirty-nine injections. Fifteen, or 46.8 per cent, of this subgroup had negative serologic reactions during the last four or more years of observation. There was 1 case of aortitis. The last of the subgroups, in which there were 21 patients, received more than one hundred and forty injections. Five of these patients, or 23.8 per cent, had negative serologic reactions during the last four or more years of observation. There were no complications.

The data show that the amount of heavy metal received had no appreciable effect on the serologic outcome. The percentage of patients with negative reactions during the last four years of observation was approximately the same for the group which received forty to sixty-nine injections of a heavy metal as for the group which received seventy to ninety-nine injections. The percentage rose in the group which received one hundred to one hundred and thirty-nine injections but fell again in the group which received one hundred and forty or more injections. Thus, from a serologic standpoint, little is to be gained by prolonged therapy with a heavy metal. From a clinical standpoint, the complications were fairly evenly divided between the four groups, and there was no decided preponderance in the group which received the smallest amount of heavy metal therapy. From these studies, therefore, arsenical drugs seem more important in preventing serious late complications than do heavy metals. Our observations concurred with those of Discker, Clark and Moore in this regard. These authors found that the highest percentage of complications occurred in patients receiving little arsenical therapy.

Howe's<sup>6</sup> studies on the pathologic appearance of the aortas of treated and untreated patients with syphilitic aortitis who die from any cause showed that the amount of cellular infiltrate in the aortic wall bore an inverse relationship to the amount of arsenical that the patient had received. There was little correlation with the intensity of treatment with bismuth or mercury.

We were unable from our studies to determine the exact optimum amount of heavy metal therapy, but forty to sixty injections seems adequate and probably more than necessary. We do not believe that prolonged bismuth therapy, as recommended by Kahn and Becker, is advantageous from a clinical or serologic standpoint, and the observations of Howe suggest that heavy metal therapy does not cause involution of an active syphilitic pathologic process in the aorta. We therefore believe that more emphasis should be placed on arsenical therapy for a patient with latent syphilis.

6 Howe, E. S. The Microscopic Appearance of the Aorta in the Treated and Untreated Cases of Syphilitic Aortitis, *Am J Syph, Gonorr & Ven Dis* 27:50 (Jan) 1943.

## CONCLUSIONS

1 There is a decided tendency for the blood serum of persons with untreated or poorly treated latent syphilis to fluctuate over a period of years

2 The reversal of the serologic reactions of the blood of untreated or poorly treated patients with latent syphilis to negative on single or even repeated examinations does not necessarily mean spontaneous serologic cure

3 The serologic reactions of approximately 25 per cent of untreated or poorly treated persons with latent syphilis become negative spontaneously and remain so over a period of years

4 In 20 to 25 per cent of untreated or poorly treated persons with latent syphilis belonging to mixed racial groups, including Negroes, some cardiovascular complication will develop when observations are made over a period in excess of thirteen years

5 There is a definite relationship between the state of the serum in poorly treated or untreated persons with latent syphilis over a period of years and the ultimate clinical outcome. Persistence of strongly positive serum predicts a poor clinical outcome, whereas tendency to fluctuate indicates a relatively good clinical outcome

6 Frank early syphilis does not confer special immunity to late complications

7 There is a decided tendency for the blood serums of persons with well treated latent syphilis to fluctuate over a period of years

8 Adequate antisyphilitic treatment of persons with latent syphilis results in only a 17 per cent increase in long term serologic reversals over those that occur spontaneously with little or no treatment

9 Adequate antisyphilitic treatment reduces the hazard of late serious complications to a minimum

10 There is no relationship between the state of the blood serum in persons with well treated latent syphilis and the development of late complications

11 Arsenical drugs are more efficacious in preventing late complications than heavy metals

12 Twenty to twenty-nine injections of an arsenical is adequate therapy. This should be combined with alternating courses of a heavy metal. More than this amount does not result in any reduction of complications

13 Forty to sixty injections and, possibly less, of a heavy metal are adequate. This should be combined with adequate arsenical therapy. Further heavy metal therapy does not reduce the likelihood of late complications

## ABSTRACT OF DISCUSSION

DR UDO J WILE, Ann Arbor, Mich This is a valuable paper I wish that one could study these figures a little bit more at leisure, so that one could get the correct interpretation of them, or at least have them interpreted a little more fully

I want to ask one question What became of the persons with neurosyphilis? There is no mention made in the discussion of all these patients who have been treated with regard to the incidence or accident of neurosyphilis All that have been mentioned are the persons with cardiovascular syphilis

Were there any patients, for example, who acquired tabes, paresis and visual symptoms of one kind or another?

DR HAROLD N COLE, Cleveland There is a real need for careful studies on groups of syphilitic patients followed over a long period It is for that reason that this study of Drs Jordon and Dolce is so important It helps to answer some of the unanswered questions that have arisen in various surveys of different types of syphilis Thus, the Cooperative Clinic group, in their report on cardiovascular syphilis, emphasized this very item, that long-continued follow-up might certainly show that apparently well persons would succumb to cardiovascular complications That is the point brought out by the authors

It is seldom that any clinic can present data on 169 patients with latent syphilis observed ten years or more The authors do well to emphasize the variability of the results of serologic examinations of the blood

As they well show, in latent syphilis it is not serologic reactions that tell the story so much as the amount of treatment, yet they do emphasize the importance of a persistent, strongly positive serologic reaction of the blood as indicating a poor clinical outcome

There are other most important observations From 20 to 25 per cent of untreated or poorly treated persons with latent syphilis in mixed racial groups will have some cardiovascular complications when observed over a period of thirteen or more years They also find that adequate antisyphilitic treatment reduces the hazards of late serious complications to a minimum

I am surprised to note that the authors' data show arsenical drugs to be more efficacious in preventing late complications

The Cooperative Clinic Group seem to have the idea that heavy metal, in the form of bismuth, helped a great deal in preventing these late complications But here, again, the main point brought out is that it is the well treated patient that is far less liable to these crippling or even fatal complications than the one given irregular, inadequate therapy

Again, there is another word of warning A patient supposedly free from involvement of the central nervous system, both by physical examination and by lumbar puncture, fourteen years later reports with paresis This patient, however, was in the poorly treated group

The authors are to be congratulated on this careful, most laborious, five year investigation Only one who has gone through such a study can realize the enormous amount of work and detail involved

DR PAUL A O'LEARY, Rochester, Minn Late latency has probably caused more concern to the physicians who treat syphilis than any other form of the disease, because there have not been established sufficient criteria on which to base a rational therapeutic procedure for it I have used the following three factors as a guide in determining the need for treatment in these patients first, the duration of the syphilis in the patient, second, the age of the patient, and,



third, the amount of previous treatment the patient has received. I still feel these are significant guides, in that an elderly patient who has had latent syphilis for many years and who has been given fifty or more injections of an arsenical and a heavy metal is entitled to parole from further treatment, and, by the same token, a young patient with syphilis of ten years' duration who was treated haphazardly is in need of continued treatment, even though his disease is in the phase of latency.

I feel as Drs. Wile and Cole do, that this is an important contribution, because we have been under the impression, as a result of previous studies, that late latency is a safe state of syphilis for the patient.

It is important that Dr. Jordon's patients be followed from now on for at least another ten years, because no one has as yet had the opportunity to follow a sufficient number of patients through the life of their syphilis to know the actual significance of latency, and it is such studies as this that will give the needed information.

DR. CHARLES C. DENNIE, Kansas City, Mo. I had the opportunity of reading Dr. Jordon's paper before it was presented here at the meeting, and so I had a little more time to go over it than some of the others.

I may say, and I think that I am right, that Dr. Jordon determined that all these patients had negative cerebrospinal fluids before he began the study. I believe that in his paper he reported but 1 case in which paresis developed in a patient with positive cerebrospinal fluid in this group. So that answers one of the questions.

In the first place, latency is determined not histologically but chronologically—early latency and late latency. The latter means after five or more years. Hence, since there are no good criteria for determining the condition, what is latency in syphilis and is it really latency? No, it is not, because these figures that the authors have given, showing a large percentage of involvement of cardiovascular syphilis during the course, especially of the untreated patients, show that in the majority of these cases there is no such thing as latency.

Also, there are no very accurate methods of determining whether or not these patients have signs or symptoms. In persons with congenital syphilis one has a much better opportunity to determine that type of activity, for one can look into the eye. It has been determined in our clinic, in over 1,600 children with active congenital syphilis, that each child has an average of 42 per cent of definite syphilitic changes in his eye. The eye is the only place where one can look in the determination of this.

In the case of an adult one might look into the bladder or into the stomach or into the rectum, but if one were able to look within the aorta, one would find that a large percentage of these patients had the organisms there.

Another point also brought up is that in these cases of latency the organism has time to become set in the patient. As has been shown many times here, it has long been the concept of the syphilologist that the adequate treatment of early syphilis has met with more success than any other type of treatment. That means that these organisms, which are so widely spread during the disease, have reached the places they are going to affect in later life and there entrench themselves. Scar tissue and fatty tissue are the final end of the pathologic condition.

Then enters the immunity of the body itself, the immunologic factor, which determines to a large extent when this disease will fluctuate upward or downward. To my mind, that is the explanation of the fluctuation of the titer of the syphilitic substances in the blood. At times the immunity of the patient is high, at times it is low.

We can see this phenomenon in the children with congenital syphilis in the so-called mixed families, in which the first child is sound, the second child is not sound and the third child is again syphilitic. Families are seen in which healthy children and syphilitic children occur, which shows the fluctuation of the immunologic factors of the human body if the syphilis is one of a fluctuating nature.

Bruusgaard, in the 309 cases of living persons who were known to have been syphilitic at one time, found that 27.9 per cent of them were free from the disease after ten to forty years. He did not examine the cerebrospinal fluids. In reviewing the autopsy records which he was fortunate enough to secure, he found that the vascular system was most often affected.

These observations point to the belief that the stronghold of *Treponema pallidum* is in the aorta and in the testes.

Care of the patient with latent syphilis demands that the patient be followed through life. This must be done not only by the physician alive at the present time but by the one who takes up his practice, because many of these syphilitic patients will live through the lives of both of these men. The problem finally boils itself down to the fact that some more accurate method of diagnosis of latent syphilis must be developed. Some method must be developed by which one can find out whether the disease is active when it is thought to be latent, because, I believe in most cases latent syphilis really is slowly active.

I think that the authors of this paper are to be congratulated for bringing up a subject which confuses the general practitioner more than any other he has.

DR SAMUEL E. SWEITZER, Minneapolis. I have wondered, in view of the modern therapy of syphilis and the high incidence of cardiovascular involvement that Dr. Jordon has reported, whether the intermittent treatment that so many patients still get is not responsible for this cardiovascular involvement.

One drug that has been almost dropped from the armamentarium of the therapy of syphilis and that is no longer emphasized, particularly for cardiovascular syphilis, is potassium iodide. It will be found that if these patients are given potassium iodide better results will be obtained than if only arsphenamine and bismuth are used.

DR JAMES W. JORDON, Buffalo. Because of the time element I had to leave out many things which are included in the paper. I did not define very well what I meant by latent syphilis, when the term "latent syphilis" is used in this paper, it means that either the spinal fluid was not examined or if it was examined it was normal. Ninety-four of the 100 well treated patients had their spinal fluids examined, and they were normal. If we found any patient with asymptomatic syphilis and a spinal fluid positive for the disease, he was considered to have asymptomatic neurosyphilis. The cases of these patients were not included in the paper.

DR UDO J. WILE, Ann Arbor, Mich. Were the examinations of the spinal fluid repeated in the beginning?

DR JAMES W. JORDON. Many of the patients had more than one examination, many of the 69 poorly treated patients refused to have their spinal fluids examined. Examinations of the spinal fluid were made for 29 of the 69 poorly treated patients. Any of this group who had a positive spinal fluid were not included in this study, and any patient who did not have the spinal fluid examined and subsequently had neurosyphilis was likewise rejected from this study.

We were able to follow these patients over a period of years because one of the larger hospitals takes care of the medical and dental needs of a large proportion of the indigent people in Buffalo. They report back to the hospital or to the

clinics for numerous minor ailments, and each time they report they are referred back to the syphilologic department if there is a history or physical condition suggestive of syphilis

There was 1 case of paresis, this case was included in the paper because at the time of the original examination an examination of the spinal fluid showed it to be normal. Fourteen years later, when paresis developed, the spinal fluid was strongly positive

From this study it is apparent that we have been partial to the use of large amounts of bismuth in the treatment of latent syphilis. Our well treated patients received an average of seventy-eight injections of a heavy metal. We were surprised from our study to find that arsenicals seemed more effective than bismuth in the prevention of late complications. We have probably in the past overtreated patients with bismuth. Moore has expressed the belief that bismuth therapy has been overemphasized in the treatment of latent syphilis. It is interesting to note that Howe found that the amount of cellular infiltrate in the aortic wall of patients who died after having syphilis bore an inverse relationship to the amount of arsenical therapy the person had received. He found there was almost no relationship to the amount of bismuth. This confirms from the pathologic standpoint what we have observed from the clinical standpoint

Regarding the use of iodides, very few if any of our patients receive iodide therapy. We have not used iodides routinely in our clinics in the treatment of syphilis

## PENICILLIN IN DERMATOLOGY

A Study of One Hundred and Seventy-Four Cases

CAPTAIN ORLANDO CANIZARES \*

MEDICAL CORPS, ARMY OF THE UNITED STATES

THE remarkable antibacterial properties and the relatively low toxicity of penicillin make it a logical agent to use against cutaneous pyogenic infections

Penicillin, in local applications, was first used by Fleming as early as 1929<sup>1</sup> Florey and Florey<sup>2</sup> stated "In essence, the problem of using penicillin locally is that of devising some means to apply a very soluble and diffusible substance so that a bacteriostatic concentration is constantly maintained at every point where there are infecting organisms" The local use of penicillin in the treatment of burns and scaldings was satisfactory with a freshly prepared cream of penicillin<sup>3</sup> One of the earliest reports on the use of penicillin in dermatology was made by Roxburgh, Christie and Roxburgh<sup>4</sup> They reported satisfactory results in cases of sycosis barbae, impetigo, blepharitis and also some cases of eczema with secondary infection Sophian and Connolly<sup>5</sup> found topical applications of penicillin excellent in sycosis barbae and furunculosis The selection of the proper base for the use of penicillin locally is a problem which has not yet been solved A  $p_H$  of about 7 seems to be essential for the preservation of the activity

\* Instructor in Dermatology, New York University College of Medicine, on leave of absence

Read at the Army Air Forces Rocky Mountain District Medical Conference, Army Air Forces Officers Replacement Depot, Kearns, Utah, May 15, 1945

1 Fleming, A On Antibacterial Action of Cultures of *Penicillium*, with Special Reference to Their Use in Isolation of *B. Influenzae*, *Brit J Exper Path* **10** 226-236 (June) 1929

2 Florey, M E, and Florey, H W General and Local Administration of Penicillin, *Lancet* **1** 387-397 (March 27) 1943

3 (a) Clark, A M, and others Penicillin and Propamidine in Burns Elimination of Haemolytic Streptococci and Staphylococci, *Lancet* **1** 605-609 (May 15) 1943 (b) Bodenham, D C Infected Burns and Surface Wounds Value of Penicillin, *ibid* **2** 725-728 (Dec 11) 1943

4 Roxburgh, I A, Christie, R V, and Roxburgh, A C Penicillin in Treatment of Certain Diseases of Skin, *Brit M J* **1** 524-528 (April 15) 1944

5 Sophian, L H, and Connolly, V J Use of Penicillin in Topical Application, *Am J M Sc* **208** 577-580 (Nov) 1944

The ideal base is one which will bring the penicillin into contact with the bacteria and will maintain its potency for a reasonable period

This report deals with a series of 174 patients with cutaneous diseases mostly pyogenic in origin, treated at an Army Air Force Regional Station Hospital. It includes both patients who were hospitalized and those treated at the outpatient clinic. All cases were closely supervised and followed for a period varying from three weeks to six months. In all cases reported only penicillin preparations were used, unless otherwise stated. Bacteriologic study of the cases, to determine the causative organism and its sensitivity to penicillin, was made whenever possible. Penicillin was applied locally in the great majority of the cases. In a few cases, in which a systemic effect was desired, 200,000 units was injected intramuscularly. The following penicillin preparations were used: (a) penicillin solution, 500 units per cubic centimeter, (b) penicillin in petrolatum and hydrous wool fat, 500 units per gram, (c) penicillin in water-soluble base, 500 units per gram,<sup>6</sup> (d) penicillin dissolved in equal parts of water in an emulsion base, 250 units per cubic centimeter. All preparations were kept in the refrigerator.

The selection of the preparation depended entirely on the stage of the eruption and on its location. In general, acute vesicular and extensive eruptions were treated with wet dressings or sprays of the solution, subacute and localized lesions were treated with emulsion and water-soluble ointment, chronic lesions were treated with the ointment containing petrolatum and hydrous wool fat. Lesions were cleaned by removing crusts and opening pustules before the applications of the penicillin preparation. For acute, extensive lesions the preparations were used five times a day. In more chronic stages the ointments were applied by massage three times a day.

6 The water-soluble base was prepared as follows

	Gm or C c
White floating soap powder	33
Distilled water	100
Cold cream (special)	267

The formula for the special cold cream is as follows

	Gm or C c
White wax	60
Spermaceti	60
Hydrous wool fat	25
Cottonseed oil	260
Sodium borate	3
Distilled water	95

The ointment was tested by the Food and Drug Administration, through the courtesy of Lieut Col J R Scholtz. It was found that three weeks after its preparation only 50 units of penicillin was present per gram. Therefore only freshly prepared ointment was used. The formula was originated by Sergeant Frank A Olson, Pharmacist.

## STUDY OF CASES

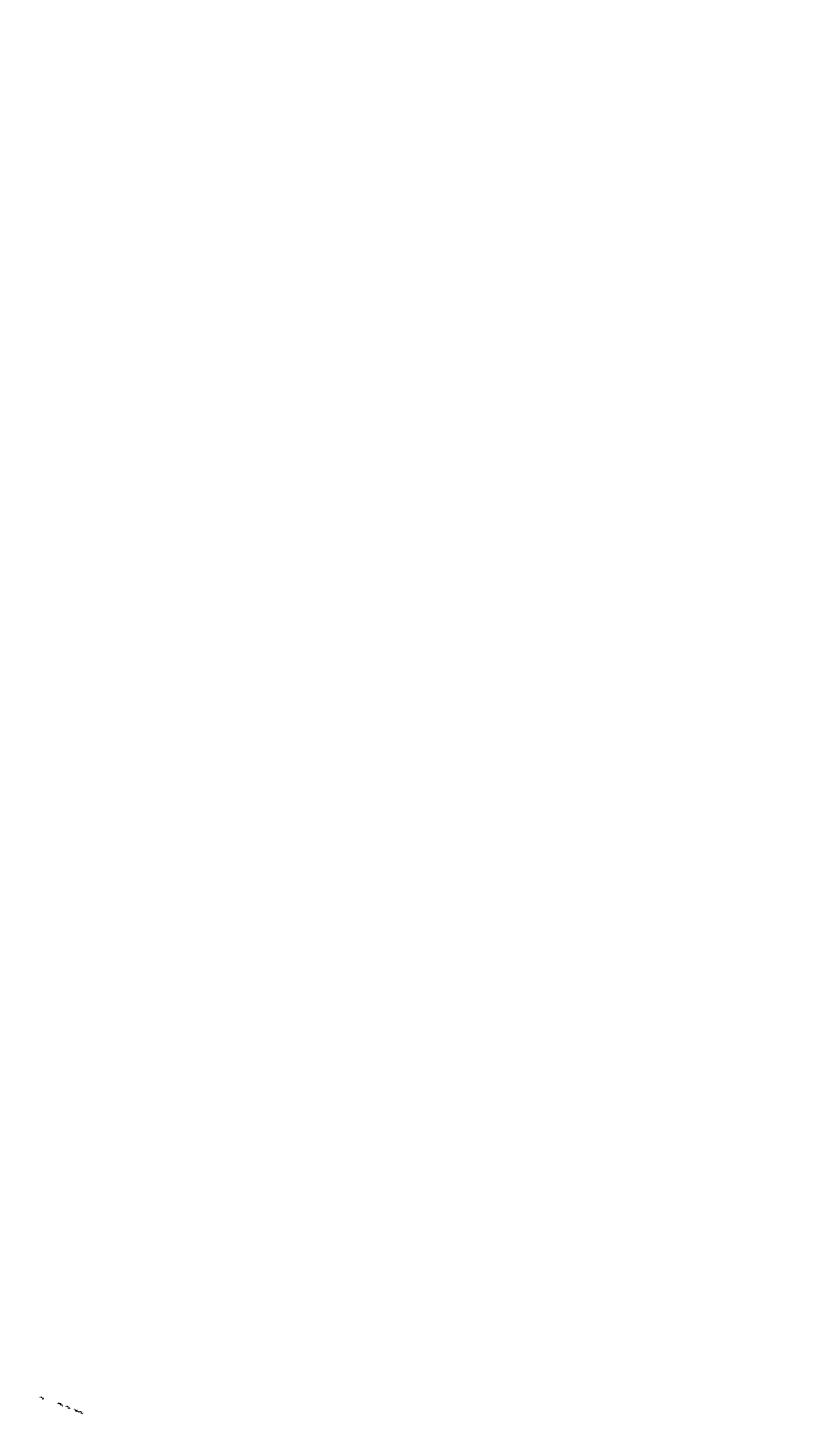
*Staphylococcic Dermatitis*—*Sycosis Vulgaris* In 16 cases, sycosis vulgaris was treated with local applications of penicillin. The duration of the disease prior to treatment varied from six weeks to eight years. In 3 instances, patients had previously received penicillin intramuscularly, without success. In most cases the disease was due to hemolytic and nonhemolytic *Staphylococcus albus*. In 6 cases the eruption improved steadily until cure, the average period required for cure was three weeks. The response in some cases was dramatic, with long-standing eruptions clearing up in three or four days. In 4 cases the lesions recurred when the treatment was discontinued, only to disappear when it was reapplied. When the application of penicillin lotion was continued for several weeks after apparent cure, no recurrences of this type were observed. In 1 case of several years' duration, a severe dermatitis developed when penicillin ointment was applied, so the treatment was discontinued. Circumstances beyond my control prevented a complete study of this case, in which the dermatitis may have been due to penicillin, to its impurities or to the ointment base. In 3 cases dermatitis due to hemolytic *Staph albus* failed to respond to different preparations and different strengths of the drug. Thus the treatment was satisfactory in 10 cases and unsatisfactory in 6. In summary, it may be said that topical applications of penicillin deserve a place in the treatment of sycosis vulgaris. The stubborn resistance of this disease to treatment and its tendency to relapse are well known. Although not successful in every instance, penicillin has proved effective in cases in which other medicaments have failed.

*Impetigo Contagiosa* In 22 cases impetigo contagiosa was treated with penicillin locally. The size of the eruptions varied from that of a dime to extensive lesions covering most of the face. In most cases the eruptions were due to hemolytic *Staph albus* alone or associated with an alpha hemolytic streptococcus. In all cases, the patient was advised to remove the crusts with soap and water. Wet dressings and sprays were used for extensive eruptions. Lotions and ointments were prescribed for limited areas. The results were good. In all except 2 cases, the eruption cleared up rapidly in from three to seven days. The 2 failures were due to the fact that a dermatitis venenata developed in the patients.

*Ecthyma* In 6 cases ecthyma of the lower extremities was treated with penicillin ointment. After the crusts were removed, the ointment was applied to the lesions by massage. Early epithelization of the lesions was noted in 5 cases. In 1 case a dermatitis venenata developed, and the treatment was discontinued.

*Infectious Eczematoid Dermatitis* In 12 cases infectious eczematoid dermatitis was treated by local applications of penicillin. In 10 cases the improvement was rapid. In 1 case recovery was slow and followed by a relapse. In 1 case the disease failed to respond to therapy. In 3 cases the eruption began with scabies. In all cases the eruption was localized on the exposed parts, especially on the neck, on the sides of the face and on the ears. *Staphylococcus aureus* was isolated in 8 cases. The average period of hospitalization required was fifteen days. Two more weeks were needed for complete recovery. The treatment was begun with solutions and continued with ointments.

*Folliculitis* In 14 cases of folliculitis of the extremities, the disease responded satisfactorily to treatment with penicillin. Two patients had previously received 100,000 units intramuscularly, without improvement. *Staph albus* was obtained in cultures in 4 cases. In 2 cases folliculitis of the back of the neck failed to improve.



dary infection of atopic eczema was not controlled by penicillin in 3 cases. In 1 of them there was an exacerbation of the eruption. In 8 cases nummular eczema responded well to penicillin ointment. Not only was the secondary infection controlled but the original condition improved considerably in 6 of them. It is to be remembered that acceptance of the possibility of the parasitic origin of this disease has been advocated. In 3 cases there was a relapse, and the eruption required further treatment. Summarizing 48 cases of secondarily infected dermatitis and eczemas of different origin, satisfactory results were obtained following treatment of the disease in 24 of them. The results obtained point favorably to the use of penicillin locally to control secondary infection and thus prepare the eruption for further treatment. The drug cannot be expected to have any effect on the original disease, with the possible exception of nummular eczema.

*Miscellaneous Diseases*—In 7 cases, acne vulgaris was treated with local applications of penicillin. Only in 1 case, in which the pyogenic factor was predominant, did the lesions improve. In 5 cases, seborrheic dermatitis was treated without improvement. In 1 case of erysipeloid of Rosenbach, a butcher was treated with 100,000 units of penicillin administered intramuscularly, after the eruption had failed to respond to sulfadiazine. The lesions cleared up entirely in four days. This favorable response to penicillin confirms previous experimental studies. In 4 cases, psoriasis failed to improve after three weeks' treatment.

#### REACTIONS

In 4 cases (29 per cent) a dermatitis venenata following the application of penicillin preparations developed. The lesions were vesicular and appeared about the area where the ointment was applied. In no case were systemic reactions noted. In 3 cases patch tests were performed with penicillin ointment and with the base after the dermatitis had disappeared. The results were consistently negative. This shows that either injury to the tissues or the mode of application of the ointment may have played a role in the production of the dermatitis. In all instances the application of penicillin ointment was discontinued.

#### SUMMARY AND CONCLUSIONS

In a total of 174 cases dermatologic diseases were treated with different topical preparations containing penicillin. Satisfactory results were obtained in cases of impetigo, sycosis vulgaris, infectious eczematoid dermatitis, streptococcic dermatitis, ecthyma, dermatitis repens and some cases of folliculitis and hidradenitis suppurativa. In half of the cases of secondarily infected dermatitis, improvement followed penicillin therapy. Nummular eczema responded well. Intramuscular administration of penicillin was associated with topical applications in cases of furunculosis. In 1 case, erysipeloid of Rosenbach was cured by the injection intramuscularly of 100,000 units of penicillin.

It is hoped that the satisfactory preliminary results reported will encourage further study of this subject. Indiscriminate use of penicillin locally should, however, be avoided. The recent experience



resulting from the abuse of local application of sulfonamide derivatives should be kept in mind

Local penicillin therapy is still in its infancy. Much work has to be done before definite indications, contraindications and dosage are established. The ideal base is still to be found. The reactions, local and systemic, should be carefully studied. The problems of sensitivity to penicillin and the resistance of different organisms to it are of paramount importance. They require methodical, clinical and bacteriologic investigation. Until these problems are solved, it would be advisable to avoid the general use of penicillin in topical applications.

# PRESERVATION OF VIRULENCE OF *TREPONEMA PALLIDUM*

## Some Additional Laboratory Methods

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SAN FRANCISCO

SINCE Bertarelli<sup>1</sup> in 1907 discovered that rabbits could be successfully inoculated with *Treponema pallidum* the rabbit testicle has been the main source of the live virulent cultures used in experimental syphilis. Kolle and Schlossberger<sup>2</sup> in 1926 found that the white mouse also could be successfully inoculated with syphilis (symptomless infection?) and after a number of days (the incubation period varying for the different organs e.g., lymph nodes, thirty days, spleen, fifty days and brain, one hundred and fifty days) these mouse tissues would produce a specific orchitis in about sixty days after injection into rabbit testicle.

During the past eighteen years laboratory strains of *S T pallidum* have been perpetuated in this manner, either by rabbit to rabbit or by rabbit to mouse and mouse to rabbit transfers. The presence of the *S T pallidum* in the various mouse organs (brain excepted) has been demonstrated by Levaditi, Vaisman and Schoen<sup>3</sup> and Vaisman<sup>4</sup> by the single section silver staining technic of Dieterle.

Turner<sup>5a</sup> in 1938 found that he could maintain the virulence of the *S T pallidum* in the frozen state ( - 78 C ) for over a year. This was a notable discovery, as it made possible the immediate availability of virulent cultures.

The following experiments are based on the observations of Kolle and Schlossberger and Turner and consist of

- 1 The direct mouse to mouse transfer of virulent mouse organs (without the use of an intervening host, such as the rabbit)
- 2 The behavior of syphilis-infected tissue (other than rabbit testicle) in the frozen state ( - 78 C )

1 Bertarelli, E. *Centralbl f Bakt (Abt 1)* **43** 448, 1907

2 Kolle, W., and Schlossberger, H. *Deutsche med Wchnschr* **52** 1245, 1926

3 Levaditi, C., Vaisman, A., and Schoen, R. *Compt rend Soc de biol* **112** 1669, 1933

4 Vaisman, A. *La syphilis inapparente experimentale chez la souris*, Paris, Edité par L'imprimerie Trancende, March 1936

5 (a) Turner, T B. *J Exper Med* **67** 61, 1938 (b) Turner, T B., and Fleming, W L. *J Exper Med* **70** 629, 1939 (c) Turner, T B., and Brayton, N L. *ibid* **70** 639, 1939

## THE DIRECT MOUSE TO MOUSE TRANSFER OF VIRULENT MOUSE ORGANS

(a) *Rabbit to Mouse Transfer*—Twelve white mice were inoculated subcutaneously with chancre grafts from rabbit testicle (Nichols' strain) on Aug 1, 1941. Six months later, Feb 3, 1942, 6 of these mice were killed, and their lymph nodes were pooled and emulsified (lymph node emulsion 1), as were also their spleens (spleen emulsion 1) and their brains (brain emulsion 1). Specimens of these three emulsions, although negative for *S T pallidum* on dark field examination, produced a specific orchitis in approximately sixty days after inoculation into rabbit testicle.

(b) *Mouse to Mouse Transfers*—Lymph node emulsion 1 was injected subcutaneously into 12 mice on Feb 3, 1942. Six mice were killed on August 25, and their lymph nodes were pooled and emulsified (lymph node emulsion 2), as were also their spleens and brains. All three emulsions were negative for the *S T pallidum* on dark field examinations, but all three produced a specific orchitis sixty days after inoculation into rabbit testicle.

Spleen emulsion 1 was injected subcutaneously into 12 mice on Feb 3, 1942. Six mice were killed on August 25, and their spleens were pooled and emulsified (spleen emulsion 2), as were also their brains and lymph nodes. All three emulsions gave negative results following inoculation into rabbit testicle. The remaining mice in this group, inoculated February 3 with spleen emulsion, were killed on November 26, and their spleen, lymph nodes and brain were injected into rabbit testicle, again with negative results (spleen experiment concluded).

Brain emulsion 1 was injected subcutaneously into 12 mice, Feb 3, 1942. Six were killed on August 25, and their brains were pooled and emulsified (brain emulsion 2), as were also their spleens and lymph nodes. All three emulsions gave negative results following inoculation into rabbit testicle. The remaining mice in this group, inoculated February 3 with brain emulsion, were killed on November 26, and their brain, lymph nodes and spleen were injected into rabbit testicle, again with negative results (brain experiment concluded).

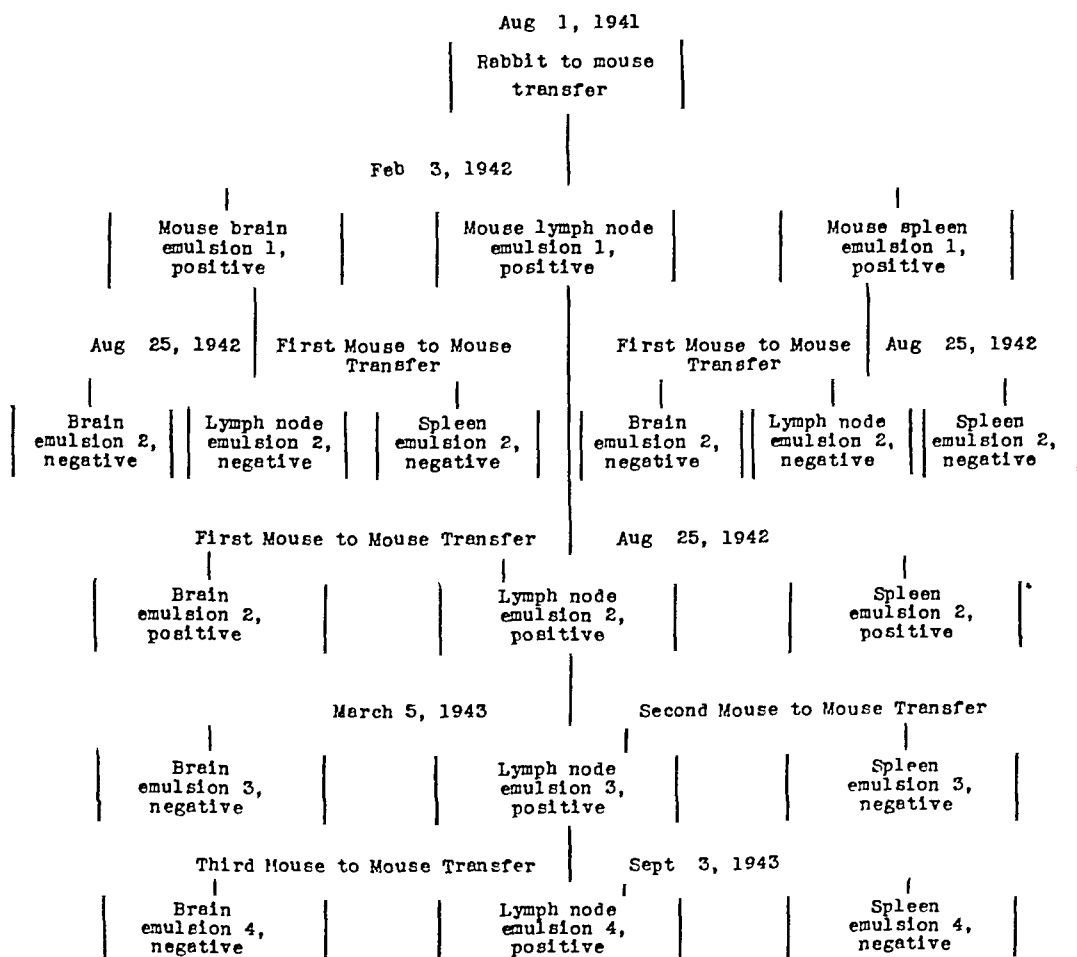
Lymph node emulsion 2 was injected subcutaneously into 12 mice Aug 25, 1942. Six mice were killed on March 5, 1943, and their lymph nodes were pooled and emulsified (lymph node emulsion 3), as were also their spleens and brains. All three emulsions were negative for *T pallidum* on dark field examination. On passage into rabbit testicle, the lymph node emulsion, however, was the only one that produced a specific orchitis.

Lymph node emulsion 3 was injected subcutaneously into 12 mice March 5, 1943. Six mice were killed on September 9, and their lymph nodes were pooled and emulsified (lymph node emulsion 4), as were

also their spleens and brains All three emulsions were negative for *T pallidum* on dark field examination On passage into rabbit testicle, the lymph node emulsion again was the only one that produced a specific orchitis (chart)

THE BEHAVIOR OF INFECTED SYPHILITIC TISSUE (OTHER THAN RABBIT'S TESTICLE) IN THE FROZEN STATE (-78 C)

The syphilitic tissue used in this experiment consisted of rabbit lymph nodes, mouse brain, mouse lymph nodes and mouse spleen



brain specimens gave negative results. Seventy days after inoculation both mouse lymph node specimens caused small indurated nodules in which an occasional *T pallidum* was found. Both mouse spleen specimens produced voluminous orchitic swellings (containing numerous spirochetes [*T pallidum*]) sixty days after inoculation.

#### SUMMARY

1 (a) Brain, lymph nodes and spleen from mice infected with syphilis were transferred directly from mouse to mouse for three transfers without an intervening host, such as the rabbit, being used.

(b) The infectivity of all organs was ascertained at each transfer through inoculations into rabbit testicle.

(c) After the first direct transfer (in which the brain and spleen as well as the lymph nodes were infectious), the lymph nodes proved to be the only one of these three organs which maintained their virulence.

2 (a) Rabbit lymph nodes, mouse brain, mouse lymph nodes and mouse spleen infected with syphilis were frozen and kept at a temperature of  $-78^{\circ}\text{C}$ .

(b) The infectivity of all organs was ascertained, both before and after the experiment, through inoculation into rabbit testicle.

(c) At the end of a year the rabbit lymph nodes and the mouse brain had lost their virulence. The virulence of mouse lymph nodes had been attenuated, but the infectivity of mouse spleen had not been impaired.

## TEMPORARY UNILATERAL LOSS OF VISION ASSOCIATED WITH IODERMA

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**I**ODIDES enter the body by ingestion, injection, inhalation, absorption from various body cavities and orifices where they have been introduced for therapeutic or diagnostic reasons and by absorption through the intact or broken skin by way of the pores.

The iodide ion replaces chlorine from various chlorine compounds. The displaced chlorine is then excreted. This is a reversible mechanism, since an increase of chlorine intake will by mass action free the iodine ions, which are then excreted. Bromine acts in a similar way by replacing chlorine and iodine and vice versa. This is the basis for the modern treatment of both iodism and bromism.

Iodides circulating in the system rapidly reach all the tissues and structures of the body. In the blood, iodides are chiefly found in the plasma, there being but small amounts in the blood corpuscles. The thyroid gland is the chief depot for iodides normally. Any increase in iodide intake causes a rapid increase in the iodide content of this gland. One part per million is the amount normally found in other parts of the body. Iodides easily pass through the choroid plexus to reach the cerebral spinal fluid and also pass through the placenta to reach the fetus in utero. They also pass through the ciliary blood vessels of the iris to reach the chambers of the eye.

Iodides are excreted mainly by the kidneys, but they are found in the excretions and secretions of most if not all the glands of the body. The amount normally excreted is infinitesimal, but an increase in intake will cause a rapid increase. This fact is easily demonstrated in the saliva, in the mucus of the mucous glands of the upper and lower parts of the respiratory tract, in the excretions and secretions of the gastrointestinal tract, including the liver, in the sweat from the coil glands and in the sebum from the sebaceous glands of the skin. Iodism in nursing babies whose mothers are taking iodides for one reason or another demonstrates that iodides are easily secreted with the milk from the mammary glands.

The symptoms of iodism are traceable to a large extent to the irritative effects of iodine ions passing through the various glandular structures. The early prodromal symptoms, nasal congestion, nausea, anorexia, rhinorrhea, lacrimation and conjunctival congestion, are due

to this excretion of iodine ions through the glands of the respiratory and gastrointestinal tracts and also due to the irritative effect on the mucous membranes after excretion. Acneform eruptions are due in part to the irritative effect of iodides on the sebaceous glands, through the indirect effect on the glands of internal secretion such as the thyroid must also be considered.

Besides the common acneform eruption and the folliculitis from iodides, less common cutaneous manifestations are also seen. These range from simple erythema through papular, vesicular, pustular, bullous, fixed pigmentary, vegetative and purpuric types. Bullous ioderma was first described by O'Rielly<sup>1</sup> in 1854. Purpuric lesions were first described by Fournier<sup>2</sup> in 1877. In 1878 Adamkiewicz<sup>3</sup> demonstrated iodides in the contents of a bullous lesion.

Deaths from iodism have not been common since Mac Kenzie<sup>4</sup> reported death from a minute dose ( $2\frac{1}{2}$  grains [0.16 Gm.]) of potassium iodide with purpuric lesions in 1879. Pusey<sup>5</sup> described fatal ioderma in a nursing baby from iodides from the mother's milk in 1911. Hollander and Fetterman<sup>6</sup> reported what they considered the eleventh fatal ioderma in the literature in 1936. Goldburgh and Baer<sup>7</sup> reported an anaphylactic death from diodrast, and iodine-containing urinary contrast medium in 1942 and noted at least 8 similar deaths reported in the American literature. Scadding<sup>8</sup> and others have reported deaths due to iodized poppyseed oil in bronchography. Cordray<sup>9</sup> expressed the belief that these fatalities were due to faulty preparation of the contrast medium in which the poppyseed oil was not completely saturated with iodine ions.

The exacerbation of the lesions of dermatitis herpetiformis following ingestion or injection of iodides is well known.

Iodine has been used in the treatment and prevention of goiter since Comdet introduced its use empirically in 1820. His later work proved that goiter is due to a deficiency of iodine in the soil and water of goitrous areas, resulting in deficiency of this important chemical in foods grown there. The addition of small amounts of iodine to table salt and cooking salt as a prophylaxis against goiter and cretinism has

1 O'Rielly, J. *New York M. Gaz.* **5** 7, 1854.

2 Fournier, A. *Rev. mens. de med. et chir.* **1** 653, 1877.

3 Adamkiewicz, A. *Charite-Ann.* **3** 381, 1878.

4 Mac Kenzie, S. *M. Times & Gaz.* **1** 279 and 501, 1879.

5 Pusey, W. A. *J. Cutan. Dis.* **29** 309, 1911.

6 Hollander, L., and Fetterman, G. H. *Fatal Ioderma*, *Arch. Dermat. & Syph.* **34** 228 (Aug.) 1936.

7 Goldburgh, H. L., and Baer, S. *Death Following the Intravenous Administration of Diodrast*, *J. A. M. A.* **118** 1051 (March 28) 1942.

8 Scadding, J. G. *Brit. M. J.* **2** 1147, 1934.

9 Cordray, D. *Personal communication to the author.*

been developed from this theory. Stubborn acne vulgaris as well as other forms of ioderma have been traced in whole or part to this use of iodized salt. No deaths have been proved to be due to this salt. In the case reported by Eller<sup>10</sup> fatal ioderma followed the unfortunate use of potassium iodide to treat an eruption which was later found to be due to iodized salt.

Mild to severe conjunctival irritation associated with ioderma and iodism is common. Lacrimation is one of the early signs of intolerance or excessive intake. Severer changes in the eye from this drug have seldom been described. Hallopeau<sup>11</sup> described iritis and conjunctivitis from iodides in 1888. Lewin<sup>12</sup> described retinal hemorrhages and bullous retinal lesions in 1929. Goldberg<sup>13</sup> reported iritis with hypopyon and associated synechia from iodides in 1939.

Bilateral atrophy of the optic nerve from pressure on the nerve associated with orbital edema from ioderma has been reported recently in the foreign literature. The dangers from the use of mercurial preparations near the eyes of patients taking iodides are well known. The formation of the extremely irritating mercuric iodide from the combining of the mercury and the iodine ions is the etiologic agent here. The purpose of this paper is to present a case of temporary complete unilateral loss of vision associated with bullous vegetative ioderma.

#### REPORT OF A CASE

*Present Illness*—For several years a white Australian army private had been troubled with sciatica. He had received various treatments for this, both as a civilian and at various Australian army R A P stations without relief, though he had been able to stay on duty. Late in April 1944, he was given potassium iodide grains (15 [0.97 Gm], three times a day) for this sciatica. Soon afterward he began to notice nasal congestion, rhinorrhea and nausea followed by lacrimation and congestion of the conjunctivas of both eyes. This condition rapidly became worse, and on May 8, 1944 he was admitted to an Australian base hospital, where he was assigned to the ophthalmology department. A diagnosis of conjunctivitis was made. The vision in the right eye, which had been normal, began to fail rapidly at this time, the failure was believed to be due to iritis. He was seen in the dermatology department in consultation because of a vesiculopustular eruption.

*Past History*—He had never had any trouble with his eyes in the past and had never worn glasses at any time.

*Physical Examination*—Examination on May 10, 1944 revealed a poorly nourished white man of 49 who appeared at least that age. Scattered over the face, neck, arms and legs and scrotal areas, as well as in the axillas, were numerous

10 Eller, J. J., and Fox, E. C. Fatal Iododerma, *Arch Dermat & Syph* 24: 745 (Nov) 1931.

11 Hallopeau, M. *Ann de dermat et syph* 2: 760, 1888.

12 Lewin, L. *Lehrbuch der Toxikologie*, Berlin, G. Stilke, 1929, p. 106.

13 Goldberg, H. K. *Am J Ophth* 22: 65, 1939.



discrete and confluent follicular pustules and pyodermatous lesions. On the face, neck and groin were many vesicular and a few bullous lesions. A few vegetative lesions were noted in the groin and axillas.

The palpebral and bulbar conjunctivas were greatly injected and edematous, particularly in the right eye. The extraocular muscles were grossly normal. Examination of the right eye revealed a definite circumcorneal injection. This cornea was hazy and dull, the pupil was round and small and reacted sluggishly to light and in accommodation. The vision in the right eye was for moving objects only. The fundus could not be seen, and there were no synechias noted. Examination of the left eye revealed little of note, except conjunctival inflammation. The vision in this eye was 20/20, and the fundus was normal.

*Laboratory Studies*—The Kline reaction of the blood was negative for syphilis. The urine revealed a trace of albumin with a positive reaction for iodides. The sedimentation test was 34 mm in sixty minutes. The blood count was normal. No porphyrins could be demonstrated in the urine.

*Patch Tests*—A patch test with 2.5 per cent tincture of iodine elicited a slightly positive reaction in twenty-four hours. The result of a passive transfer test was negative.

*Course in Hospital*—Treatment was begun at once with 1 per cent solution of atropine sulfate to dilate the pupils, 5 per cent sodium chloride solution (50 cc in water daily) intravenously and a decided increase in iodine-free table salt by mouth.

The vision in the right eye rapidly improved, as did the bilateral conjunctivitis, until after seven days the vision was normal in both eyes, being 20/20. The fundi were normal also at that time.

The skin improved slowly. The patient was discharged to a convalescent camp after thirty days, in excellent condition, except for a persistent weeping eczematoid eruption in the groin.

*Subsequent History*—He was again admitted July 15, 1944, with a typical erysipelas of the nose and adjacent skin. This responded rapidly to sulfathiazole by mouth and compresses of solution of boric acid locally. Examination of the eyes at that time revealed essentially normal vision and no pathologic changes in either eye.

#### COMMENT

The rapid improvement in this patient and in Goldberg's patient after the cessation of the iodides points strongly to the pathogenesis in these cases being an irritative chemical iritis from the iodine ions being excreted through the blood vessels of the ciliary body into the anterior chamber of the eye. Knapp<sup>14</sup> stated the opinion that the difficulty in vision was due to keratitis and the sluggish reaction of the pupils was due to congestion of the vessels of the iris, which always accompanies a severe conjunctival congestion. This is not true iritis in his belief.

14 Knapp, A. Personal communication to the author.

## PSYCHOSOMATIC ASPECTS OF LUPUS ERYTHEMATOSUS

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FEW STUDIES have been completed on the psychosomatic implications of dermatologic disorders, especially those of a disfiguring nature. It is fairly obvious that cutaneous diseases have a definite socioeconomic significance. If the disease assumes the form of a mild reaction the social response is minimal, but if it is widespread and elicits a distinctly negative response akin to abhorrence the factor of social rejection plays a more determining role. Extremely disfiguring diseases of the face or the presenting part of the body, such as lupus vulgaris, leprosy and syphilis and cancers, are of more infrequent occurrence. It is true that deformities of the face and its appendages occur traumatically either in civilian or in military practice, but plastic surgery generally insures a modicum of repair, and with the use of artificial prosthetics to the disfigurements there can be imparted a high degree of social acceptability. There are, however, several chronic cutaneous diseases which in a definite social milieu will arouse expressions of disgust because of a close physical resemblance, according to the layman, to socially disapproved diseases such as syphilis. In this group may be included lupus erythematosus, a reputedly noninfectious disease of a chronic nature. The strictly dermatologic aspects of this disease will not be elaborated on. However, the psychologic aspects will be given more space. Following is the report of such a case.

### REPORT OF A CASE

The patient, a veteran, had entered the service on Sept 22, 1917. While at a training camp he noted a rash, the size of a quarter, which was elevated and covered with fine gray scales, on his right cheek. He experienced neither pain nor discomfort in that region, except for a mild itching. The hair in that area ceased to grow. The rash, which was reddish, continued to extend further. The man was sent overseas and spent some time in France. After his discharge from the Army, he received treatment for his cutaneous disease, but to no avail. During the subsequent years he was treated with a multitude of pastes and ointments and also with various types of radiation, without any improvement. The rash spread over both cheeks, reached as far as the chin anteriorly and

From the Veterans Administration Facility, Sheridan, Wyo. (Captain Pisetksy is now at the Veterans Administration Facility, Roseburg Ore.)

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gradually grew toward the inferior border of both eyes and toward the outer canthus of both eyes and the bridge of the nose. In 1928 he was treated with gold sodium thiosulfate, but only a slight betterment occurred. However, this form of therapy had to be interrupted because he exhibited toxic manifestations which made him lose weight. During the following years the lesions remained more or less stationary, except for occasional exacerbations, a psychologic exciting factor could not be elicited, and the complexion of the eruption changed only in relation to exposure to sun and wind. Sometimes after the patient had been outdoors the lesions appeared somewhat blanched. At the present time there are extensive erythematous lesions involving both sides of the face, including the chin, cheeks and lobes of the ears. They have progressed also below the mandible and involve the neck and the retroauricular and mastoid areas, where the lesions are nodular rather than macular and more discrete and have not coalesced completely. Posteriorly the rash displays a purplish red tinge, whereas more anteriorly there exists some desquamation of small whitish gray scales. The involved areas seem to be widely infiltrated. The nose, including the bridge, is free of any lesions. The lobes of the ears are also extensively involved with moderate desquamation. The lesions are not painful but are moderately pruritic. Facial movements are unhampered, and there is no distortion of the face, although it is actually disfigured. Examination did not disclose any disseminated lesion in any other part of the body referable to this chronic disease. There has never been any evidence of Libman-Sacks disease.

The patient's personal psychologic reaction to his disease has varied. At the onset, when he believed that the lesions were transitory, he disregarded them entirely and, inasmuch as he was essentially extrovert in his habits, he continued his usual social pursuits. But as time went on and the lesions became more extensive, he was more frequently exposed to the taunts and jibes of his friends and co-workers. Knowing that he had been in France and that he had visited Paris, they attributed his cutaneous disease to syphilis and made him aware of their suspicions. He attempted to disregard their insinuations, but he became more sensitive and gradually more seclusive. In pursuing his occupation as a ranch hand, even though working in relatively isolated areas, he had to contend with the prejudice and antagonism of the other men who lived in the close confines of the bunkhouse with him. The same washing utensils had to be shared, and the men were loath to use them with him. The sight of his face was frequently enough to influence a prospective employer to turn him down, and he was intermittently unemployed for that reason. He was also rebuffed socially, although most people liked him personally, the distasteful appearance of his face precluded his being invited by former friends. Women usually refused to have dates with him, and, as a result, his organ inferiority became accentuated. When he was fortunate enough to go out on a rare date, he was self-conscious and ill at ease, and it generally climaxed in a moderately depressive state. He occasionally visited prostitutes, but they also had some qualms about accepting his favors. This sexual thwarting only intensified all his feelings of insecurity. As one treatment after the other proved unsuccessful and he realized that his disease would be chronic or perhaps permanent, he became bitter. Mildly paranoid ideas made their appearance, but his seclusive-

ness prevented him from giving vent to them often. He was eventually forced to attempt to set up a small cattle business for himself so that he could work independently of others and live alone. This permitted him to reduce his human associations and get along marginally. His feelings of inferiority persisted, and he continued to believe that people considered his disease filthy, infectious and disfiguring. He became lackadaisical in his attitude toward any therapy.

## COMMENT

Not only do the appendages possess the attributes of the body image but the body surface itself—that is, the skin—plays a great role in the tridimensional self evaluation. Any alteration in the texture, continuity or color of the integument creates a dislocation in the preexisting pattern of the body image and may possibly serve as the focus of origin for a sense of inferiority or social insecurity. Inasmuch as society's demands for physical perfection are stringent, decided deviations from the norm established for a given locality or larger sphere of social influence may precipitate the reaction of not belonging. Every one is acquainted with the anxiety and despondency engendered during the storm and stress period of adolescence when a crop of ugly *acne vulgaris* pustules looms hatefully prior to a much coveted party. The social reaction to and the disapproval of the ubiquitous and frequent *acne vulgaris* lesion is too well known. The more mysterious and less known cutaneous diseases provoke more pronounced negativistic judgments. In other words, the integrity of the body image produces social acclamation and praise, whereas imperfections can culminate in criticism and rejection.

Bender,<sup>1</sup> who studied the influence of somatic diseases, especially those which distort the physical structure, on the genesis of psychoses found that the mechanism was dependent on "(1) the discrepancy between the constitutionally embedded and socially determined concept of the body image and the actual physical personality or body structure determined by the pathologic process, (2) the mysteriousness and obscurity of the disease which is not understood by the patient and not experienced by him in any one but himself, (3) the thwarting of the adult social, industrial and heterosexual adaptations, which are the strivings that are patterned after the normal postural model but cannot be realized by the distorted body."

It is true that this report has not been dealing with a psychotic person, but the underlying mechanisms are the same. Lupus erythematosus has been considered a mysterious and etiologically unsolved disease, and one cannot but wonder that the patient should be overwhelmed by the rarity of the disease and the reasons for having been chosen by Mother Nature as the victim of an unusual biologic experiment. The

1 Bender, L. Psychoses Associated with Somatic Diseases That Distort the Body Structure, *Arch Neurol & Psychiat.* 32 1000 (Nov.) 1934

chromicity of the manifestations also tended to dispel any hope of amelioration. This situation also perpetuated the thwarting of social, economic and heterosexual striving and produced a moderate depressive state, chronic feelings of inferiority and a desire to remain withdrawn and seclusive rather than to attempt to obtain satisfaction of the libido.

Bender<sup>1</sup> considered somatic disturbances in the musculoskeletal system which "cause an insult to the physical personality which the subject finds difficult to accept." Roth<sup>2</sup> has discussed the distortion of the body image which accompanies the presence of edema. He found that there existed a "tendency to reject and disown the edematous parts of the body" and to project onto others the responsibility for the disfigurement of the body. It is probable that disturbances which mar the external integument follow essentially the same psychopathologic pattern. In this connection it may be well to remark that Rome and Fogel<sup>3</sup> in their discussion on the psychosomatic manifestations of filariasis might have approached their problem from the point of view of the distortion of the body image, produced by the extraordinary enlargement of the the genitals in this disease. In an analysis of the psychopathologic symptomatology these authors mentioned that anxiety, personality contraction with guilt, neurasthenic symptoms, organ preoccupation, hypersensitivity, worry, incapacity for work and disturbances in the psychosexual sphere are some of the outstanding features of this disease. These were essentially the symptoms recognized in my patient, except that overt neurasthenic signs were not prominent and he did not suffer from impotence.

Woolhandler<sup>4</sup> in commenting on a case of alopecia universalis, found that the patient had been compelled to exist almost as a pariah in his barracks, he was ostracized by his fellow soldiers. The patient in question was intelligent and of pleasing disposition and made every attempt to maintain his morale at a high level. Significantly, he was sent to a psychiatrist for examination because "he always stays by himself and does not associate with the other men." For many years, unfortunately, my patient found himself in a similar predicament. Both the alopecic soldier and my patient were subjected to intimate living conditions and a lack of privacy.

The question of the influence of the soma on the psyche has been touched on, but there yet remains to discover whether the psyche affects

<sup>2</sup> Roth, N. Psychoses in Patients with Edema, *Am J Psychiat* **100** 397 (Nov.) 1943.

<sup>3</sup> Rome, H. P., and Fogel, R. H. The Psychosomatic Manifestations of Filariasis. *J A M A* **123** 944 (Dec 11) 1943.

<sup>4</sup> Woolhandler, N. W. Dermatology in an Army Station Hospital, *Arch Dermat & Syph* **49** 91 (Feb) 1944.

the soma in lupus erythematosus. Relatively little work has hitherto been carried out on this problem, but there exists an excellent pioneer work in this field, reported by Greenhill and Finesinger<sup>5</sup>. They studied the effect of emotional factors in a series of patients with atopic dermatitis and used a series of 16 patients with lupus erythematosus as a control group. Both series of patients were subjected to a questionnaire and personal psychiatric interview. Various psychoneurotic symptoms and personality traits, such as neurotic symptoms in childhood, hysterical, anxiety, phobic, compulsive and obsessive symptoms, feelings of hostility, exhibitionistic and depressive tendencies, feelings of inadequacy, effects of emotional states on the skin, and other environmental and emotional situations, were investigated. They concluded that psychoneurotic symptoms were more prevalent in patients with atopic dermatitis than in those with lupus erythematosus and that phobic and compulsive-obsessive symptoms were commonest in both, although less decided in the patients with lupus erythematosus. They also found that unpleasant situations connected with family problems, illness, economic insecurity and trauma occurred oftener with exacerbations in the patients with lupus erythematosus. It must be admitted that depressive feelings, sensitivity, anxiety, feelings of inadequacy and hostility toward the family were present in the patients with lupus erythematosus but not nearly with the same percentage of occurrence as in those with atopic dermatitis. My patient was not cognizant of the effect of his emotional problems on his cutaneous lesions and never associated a flare-up with his difficulties of adjustment.

These considerations are practically important not only for the person who possesses an obnoxious cutaneous disease but also for the physician who must mitigate the effects of social disapproval by rational chemotherapy and solicitous psychotherapy. The economic future and the economic independence of the patient depend on his ability to cope with the feelings of inferiority and depression which are engendered. Many persons, all too conscious of their disturbed body image, are frequently inclined to shrink from social contacts and withdraw to an isolation in which they are not basically at home. This inclination must be vehemently counteracted to prevent them from magnifying the implications of their disabilities. Persuasion, verbal encouragement and enlightening talks, not too scientific and technical, on the nature of cutaneous diseases, will do much to dispel a pessimistic attitude. In severe cases more drastic psychotherapeutic measures will have to be adopted.

5 Greenhill, M. H., and Finesinger, J. E. Neurotic Symptoms and Emotional Factors in Atopic Dermatitis, *Arch. Dermat. & Syph.* 46: 187 (Aug.) 1942.

## SUMMARY AND CONCLUSION

The psychosomatic implications of chronic lupus erythematosus are presented. It is stressed that a disfiguring cutaneous ailment may produce a disturbance in the pattern of the body image, which gives rise primarily to psychoneurotic symptoms, such as anxiety, depression, feelings of inferiority, particularly in the psychosexual sphere, and insecurity. Facial disfigurement has both economic and social implications, and various degrees of psychotherapy may be indicated to establish adequate adjustment for the patient.

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# DELUSION OF PARASITOSIS

(Acarophobia)

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**A**CAROPHOBIA, parasitophobia and dermatophobia are terms employed by English-speaking dermatologists to designate a psychic state in which the patient believes that his skin is infested with some parasite. It has been loosely classified as an obsession, a phobia, a neurosis or a mania. Little attempt has been made by dermatologists or psychiatrists to define it further. The English dermatologic literature is singularly lacking in any observations on the subject. American dermatologists have contributed articles to the psychiatric literature dealing with the cutaneous psychoneuroses, among which the present subject is included.<sup>1</sup> The foreign literature contains a few noteworthy articles, one in German, by Ekbom,<sup>2</sup> being the most detailed. The disease is much commoner than the paucity of the literature would indicate.

This paper is intended to serve three purposes.

1 To present evidence to show that the term "acarophobia" is a misnomer, and to attempt to suggest a better name.

2 To outline the distinguishing features of the various abnormal mental states in which these symptoms may occur. This should be of interest to the dermatologist and should, perhaps, help him to make an approximate psychiatric diagnosis. This diagnosis would help him to decide on the proper disposition of the case and thus to minimize the disturbance that patients displaying these symptoms produce in an office routine.

3 To present a review of the literature together with a tabulation of 51 cases, including 6 previously unpublished ones of our own.

From the Department of Dermatology, Division of Medicine of the University of California.

1 (a) Eller, J. J. Neurogenic and Psychogenic Disorders of the Skin, *M. J. & Rec.* **129** 675-679, 1929. (b) Klauder, J. Cutaneous Neuroses, with Particular Reference to Psychotherapy, *J. A. M. A.* **85** 1683-1690 (Nov. 28) 1925. (c) Psychogenic Aspects of Skin Diseases, *J. Nerv. & Ment. Dis.* **84** 249-273, 1936.

2 Ekbom, K. A. Der præsente Dermatozoenwahn. *Acta psychiat. et neurol.* **3** 227-259, 1938.



## TERMINOLOGY

In the "Standard Nomenclature of Disease" (American Medical Association, 1942, p 508) the only name listed for this condition is "acarophobia." Both components of the term are inaccurate. The first root implies that the inciting parasite belongs to the zoologic order acarina or to its smaller subdivision, the family Acaridae. The second root, "phobia," implies "any persistent morbid dread or fear." These patients seldom attribute their disease to this limited group of parasites, and they do not have a fear of these organisms but are firmly convinced that they are already infested with them.

The entire range of commonly known mites and insects has been implicated at one time or another. Worms, bacteria and other "little black living objects" as well as fungi have been designated as the suspected cause of the disorder. The real or imaginary type of parasitic life selected by the patient often depends on the knowledge he possesses regarding parasites. The word "parasite," defined as a plant or animal which lives on or within another living organism, seems to cover all cases. The term "parasitosis," defined as "infestation with parasites," would be a satisfactory designation. The term "parasitism" is objected to because it has the additional meaning of "state of being parasitic." "Parasitosis" also parallels the common designations for other parasitic infestations of the skin, such as pediculosis and dermatophytosis.

Patients with this disease have no fear of becoming infested with parasites. They seldom display the hysteria and terror which the victims of true phobias exhibit. The term "phobia" is misapplied, as has been pointed out by Ekblom.<sup>2</sup> The designation "delusion," which is defined as "a false belief regarding the self," seems to describe the mental aberration observed in these patients. "Parasitosis delusion" would describe the condition, but this term makes use of two nouns, one Greek and the other Latin. Furthermore, the second word should be in the genitive case. "Delusion of parasitosis" overcomes the latter objection and is suggested as an appropriate name.

The term "delusion of parasitosis" is more applicable than "acarophobia." The designation suggested by Ekblom,<sup>2</sup> *Dermatosenwahn* (delusion of animal life in the skin) is similar. He used the adjective *parasmit*, and although this term was applicable to his group of cases, the disease is not always limited to older patients. The proposed name is short and descriptive, is recognizable by foreign-speaking peoples and should be easily found in any alphabetic tabulation of medical literature. The material at present is under many headings with scarcely any 2 articles in the same alphabetic location.

"Delusion of parasitosis" is a symptom complex and not a disease entity, although it frequently may stand alone as the only recognizable abnormal element. It is not sharply delineated from other delusions.

but merges imperceptibly with them Weidner<sup>3</sup> cited a case, not included in our tabulation, in which the patient believed that the insects were all through her house, eating it up She found small holes in the furniture and floors and enlarged them to dig out the parasites She worked incessantly every day with chemicals at the task of destroying them At no time, however, did these parasites ever trouble her own body In case 8 in our table<sup>4</sup> the patient had a "worm in her stomach" in addition to her dermal delusion Again, in other patients one finds the delusions of infection, for example, with syphilis, leprosy or tape-worms Similarly, delusions exist covering the entire scale of which the human imagination is capable It may seem unnecessary to deal at length in this communication with such an isolated bit of so large a problem, but delusion of parasitosis is the most interesting one to the dermatologist and some of the facts presented here may apply equally well to other delusions

#### PSYCHIATRIC DIAGNOSIS AND CLASSIFICATION

The exact psychiatric diagnosis and classification of patients who exhibit the delusion of parasitosis are not of much concern to the dermatologist However, a condensed discussion of this subject in the dermatologic literature should prove valuable in that it would afford a better understanding of the prognosis and the manner of disposal of such patients Liberal use has been made of textbooks on psychiatry<sup>5</sup> and the pertinent literature has been reviewed<sup>6</sup> An attempt has been made to eliminate controversial opinion in the interest of simplification and no doubt this has been carried out too completely from the psychiatrists' point of view However, the following résumé should serve as an adequate guide to the dermatologist until the patient can be placed under appropriate psychiatric care The classification employed here conforms to that of Kraepelin<sup>7</sup>

3 Weidner, H Beiträge zur Kasuistik des Ungezieferwahnes, München med Wchschr 83 1920-1921, 1936

4 Giacardy, P Case of Familial Acarophobia, J de med de Bordeaux 95 479-480, 1923

5 (a) Bleuler, E Textbook of Psychiatry, translated by A A Brill, New York, The Macmillan Company, 1942 (b) Braude, M The Principles and Practice of Clinical Psychiatry, Philadelphia, P Blakiston's Son & Co, 1937 (c) Henderson, D K, and Gillespie, R D A Textbook of Psychiatry, ed 2, London, Oxford University Press, 1930

6 (a) Rothman, S Jucken und juckendene Hautkrankheiten, in Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930 vol 14, pt 1 (b) Sack, W T Syche und Haut ibid, 1933, vol 4, pt 2

7 Kraepelin, E Psychiatrie, Leipzig, Johann Ambrosius Barth, 1915, vol 4, pt 8

The delusion of parasitosis may occur in four psychiatric entities

- A Toxic psychosis
- B Dementia precox, paranoid type
- C Involutional melancholia
- D Paranoia and paranoid conditions

Each of these will be discussed separately, with its diagnostic features, prognosis and treatment. The obsessional ideas of the psychoneurotic patient are not true delusions because the patient has sufficient insight to realize that the condition does not actually exist, nevertheless he feels compelled to react to it. Hence, the psychoneuroses and obsessive compulsive states are not included here.

*A Toxic Psychosis*—Under the stress of any severe acute or chronic physical illness or, in many instances, of drug intoxication, mental aberrations may occur. They may be anticipated in patients suffering from pneumonia, cardiac decompensation, cocaineism and acute alcoholism. It is probable that delusions of parasitosis occur commonly in this group, if isolated statements by patients are given diagnostic credence. However, these delusions are not usually systematized or "fixed." The single delusion in which we are interested may occupy the patient's mind for only a short time, perhaps no longer than a few moments, after which some other fantasy succeeds it. Such cases, of course, do not find their way into the literature pertaining to this delusion.

There are only 3 cases in our table which apparently belong in this group. In case 6, the patient<sup>8</sup> exhibited the delusion of insects intermittently only for a few weeks while acutely ill with pulmonary tuberculosis. As his physical health improved under hospital care the delusion disappeared without psychiatric attention and did not recur, even though the patient again became ill and died of his pulmonary infection a year later. In case 40, after the patient's hypertension and cardiac decompensation had been treated for a few days, the pruritus disappeared and her belief in the "parasites" appeared to be much shaken. She returned five months later to report that she had not been bothered by "parasites" during that interval, but she was not yet entirely convinced that they were permanently gone. In this case involutional melancholia probably existed also as a predisposing factor. Case 47, to be detailed later, likewise belongs in this group.

The delusion in these cases is an isolated symptom of the underlying disease and is simply a fleeting incidental manifestation of little importance. It is apparent that the delusion itself seldom requires any therapy.

Patients in this group should be directed to appropriate and competent medical care. The dermatologist should search for causes

<sup>8</sup> Myerson, A. Two Cases of Acarophobia, Boston M. & S. J. **184** 635-638, 1921.

of pruritus and eliminate them. He should also furnish whatever information his specialty may yield contributory to the proper diagnosis of the toxic state. In addition, he should emphasize that although topical medication is permissible, it actually serves poorly and as a palliative only. He should guard the patient against the development of dermatitis through injudicious medication. Psychiatric assistance may be needed occasionally.

*B Dementia Praecox (Schizophrenia)* Dementia praecox usually becomes evident during adolescence or early adult life and is characterized by a slow, progressive deterioration of the entire personality. The paranoid type of dementia praecox, which is the only one exhibiting the delusion of parasitosis, occurs comparatively later in life, frequently even after the age of 30. Few patients with dementia praecox show the first signs of the delusion of parasitosis after the age of 40. Heredity plays an important part, in a large percentage of these patients there is a family history of mental illness. They progress slowly through shyness, sensitiveness, extreme consciousness of inferiority and hypochondriac preoccupation to actual invalidism, inactivity and depression and finally to delusions and hallucinations. Contributory and precipitating factors frequently are missing, but in some cases they are present as toxic or infectious illness, pregnancy, the puerperium, domestic and financial worries and love affairs. The most prominent feature is the emotional blunting or apathy. Physically, there is likely to be loss of weight and a general lowering of the physical health.

When a delusion of parasitosis appears within this psychiatric group it should occur in early middle age, should be accompanied with considerable family and personal past history of mental illness and should exhibit much additional mental aberration. It is impossible to estimate how frequently this delusion occurs in dementia praecox. As in the toxic psychosis group, it constitutes only a small part of the total symptom complex and patients who exhibit the syndrome are rarely reported under the designation of delusion of parasitosis. It is difficult to classify many of the cases in our series because of the lack of details, but we consider that cases 4, 5, 14, 15, 34, 37 and 51 likely belong in this group.

The prognosis must be guarded, however, many patients do readjust themselves if their disease is recognized early and if they receive proper psychiatric therapy. Institutional care with occupational therapy is a beneficial adjunct to the psychiatrist's efforts. Insulin shock therapy may be helpful. These patients should have the benefit of proper advice and treatment for any actual disease of the skin that may be present. It should be emphasized, however, that this treatment is entirely irrelevant as far as the delusion is concerned, and that the latter condition should remain entirely in the hands of the "other specialist." For example,

acne vulgaris is sometimes a precipitating factor in dementia precox of predisposed adolescents, and if untreated it constitutes a barrier against readjustment

*C Involutional Melancholia*—The climacteric, or involutional period, which must be traversed by women between 40 and 55 years of age and by men at a somewhat later age, brings mental as well as physical changes. The outstanding features of this period are fatigability, anxious depression, feelings of inadequacy and insomnia. These people appear frightened, restless and hopeless. They are correctly oriented, however, and their memory usually is good. They may exhibit considerable loss of weight.

Among the mental symptoms indecision, doubt, anxiety and fear may appear in any degree, and frequently a feeling of unreality develops. Actual nihilistic and hypochondriac delusions are often encountered. Even when not noticeable, the involutional period probably predisposes the patient toward mental aberration of this type. The attitudes acquired during this time may persist for many years and thus the period may apparently merge imperceptibly into senility without full recovery from this mental predisposition. Psychic factors, such as the illness or death of near relatives, financial worries or, more rarely, physical factors may precipitate a severer degree of the mental illness. A transient episode of actual pruritus may be transformed similarly into a delusion of parasitosis in a person so predisposed. If such a delusion is not vigorously attacked by appropriate psychiatric as well as medical measures soon after it originates, it tends to become "fixed." It is then likely to be permanent, since these patients have lost much of their adaptive capacity.

The psychiatric designation "involutional melancholia" probably includes a large percentage of cases of delusion of parasitosis in patients who have no hereditary taint and in whom no mental aberrations develop until they attain the age of 40 or more years. Again, because of lack of details in the case reports, it is difficult to classify the following cases accurately, but we consider cases 3, 16, 19, 28, 30, 35, 38, 39, 41 and 50 as probable examples of this syndrome.

The prognosis is poorer than in the first group but better than in dementia precox and the paranoid type to be discussed later. The present thought among psychiatrists is that electric shock therapy as recently developed will cure a fairly high percentage of patients in this classification and that it offers a much better prognosis than any other method of therapy previously employed.

The psychiatrist may succeed by giving the patient with mild delusions a better understanding of the development of the illness, in a general nonpsychoanalytic manner, thus lessening the effect of the disease. Case 43 is illustrative perhaps, in that the delusion apparently

had been eliminated by psychotherapy, yet, when the patient was seen some years later, she reported that the treatment had been very successful, as "the bugs had been much quieter ever since"

Psychiatric treatment is best accomplished in a hospital for mental patients, where there can be proper care of nutrition, protection against despondent suicidal tendencies, appropriate sedation, occupational therapy and regular observation by competent psychiatrists

Since a transient pruritus may be a precipitating factor for the delusion such a pruritus should be terminated, if at all possible, by appropriate dermatologic measures, and the delusion may then disappear. These patients are entitled to adequate routine search for parasites, to dermatologic diagnosis and to treatment of cutaneous lesions actually present

Laboratory tests and consultations with appropriate specialists should be performed to discover or rule out possible internal causes of pruritus, such as diabetes, icterus, circulatory diseases, allergic manifestations and lymphoblastomas. Placing the patient under the care of the psychiatrist should not, however, be delayed while this is being done, as the time lost may allow the delusion to become firmly fixed

*D Paranoia and Paranoid Conditions* Paranoia is a rare and severe psychosis characterized by the insidious development of a permanent and unshakable delusional system frequently very elaborate. If the patient's attention is shifted away from his delusions, however, he is likely to appear normal mentally. The delusions are predominantly of persecution or, less often, of the grandeur type and are frequently combined. The memory remains unimpaired. Men are affected in 70 per cent of cases. Alcoholism, syphilis, arteriosclerosis and senility may cause a condition resembling true paranoia, called a "paranoid condition" or "state." For purposes of this paper differentiation is unnecessary.

It is in this classification that a bizarre solitary delusion, such as the delusion of parasitosis, may exist without any other obvious mental aberration. The delusion becomes well "fixed" and permanent unless recognized early and attacked vigorously. Even then the prognosis is extremely poor. Complete success in the therapy of well developed true paranoia has been claimed for only some half dozen cases in the entire psychiatric literature and these are questioned by many authorities. The prognosis is perhaps slightly better in the paranoid states than in true paranoia.

The paranoid patient should be examined and treated for actual dermatologic entities and a search should be made for syphilis as a possible etiologic agent. If syphilis is present the prognosis may be somewhat improved by adequate therapy. Beyond this there is nothing

whatever that the dermatologist can do for such a patient, it is useless for him to waste his time and the patient's finances in futile attempts to convince the patient that his "bugs" are a delusion. It is worse than useless to agree with the patient that they are a reality and to attempt to "cure" him. This simply serves to deepen the patient's own conviction of their reality if any room for further "fixation" still remains. Argument, persuasion, explanation and microscopic demonstrations to the patient of material brought in as "parasites" to prove its innocuous nature are always futile. It is sufficient to tell him that parasites have not been found by the usual dermatologic methods, that his condition is thus not included in that field and that no dermatologist will ever be able to help him. The interview should be short and final.

It is in cases of true paranoia that the greatest difficulty is encountered in inducing the patients to consult the psychiatrist, with slightly less difficulty in the cases of the paranoid state. The mere mention of the word "psychiatrist" will frequently cause the patient to consult another dermatologist. The better approach seems to be to state simply that he is to be referred to a "doctor who specializes in disorders of this sort." Thereafter, he should be steadfastly refused further dermatologic consultation. Such patients are potentially dangerous in many ways. They may acquire delusions of persecution directed toward the dermatologist if long association furnishes the opportunity. For a physician who is lacking in psychiatric training to encourage return visits from such patients is likely to do more harm than good.

The psychiatrist is even better able to realize that the possibility of a successful outcome through his efforts is unlikely and he too is usually reluctant to accept such patients. He will, however, care for those who have any apparent favorable signs and, after all, these are the only ones who can be helped. He should have an opportunity to examine the patient in each such instance and to decide whether or not to accept the case. When he does not accept a case he should be asked to terminate the interview permanently, without referring the patient back to the dermatologist for further disposal. His psychiatric training enables him to word his final remarks much better than could the average dermatologist when dealing with these volatile patients, thus, a vicious cycle may often be avoided. Among our cases we consider 45, 46, 48 and 49 as instances of true paranoia and 12, 13, 18, 31, 36, 42, 43 and 44 as arteriosclerotic or senile paranoid states.

#### REVIEW OF CASES IN THE LITERATURE

In utilizing the material assembled in this study, the age, sex and marital status of the patient, the duration of the delusion, the chief

presenting symptoms, the areas of the body affected, the type of parasite blamed by the patient for the disease and the results of treatment lend themselves to tabulation. They have been recorded in the accompanying table wherever the original report furnishes such information. This table has been adapted from that devised by Ekbohm and has been augmented by the addition of many more cases. Any additional unusual or bizarre features not mentioned in the table but which are considered to be of sufficient interest are contained in the following case briefs and correspond by number to those in the table.

CASE 2—The patient was feeble-minded.<sup>9</sup>

CASE 3—The patient was a timid, sad man who spoke very little. He stated that people moved away from him immediately because of his parasites.

CASE 4—The patient acquired his delusion after an acutal episode of scabies among his own children.<sup>10</sup> The mites were described as located between the skin and flesh. The delusion lessened after two months of treatment but was again present two years later.

CASE 5—The patient had vitiligo, and his delusion was limited to the areas lacking pigmentation. Wherever he went, he observed that people would begin to scratch and slap at the insects which jumped onto them from him.

CASE 6—This patient also had vitiligo, but the delusion was not limited to the depigmented areas. The delusion was present only while he was acutely ill with tuberculosis and receded as his general health improved. He died of tuberculosis one and one-half years later, without again having the delusion.

CASES 7 and 8—The patients were husband and wife. The husband was the first to believe that the infestation was present. He believed it to be scabies contracted from one of his neighbor's servants and thence transmitted to the children of his own employer, to his own 15 year old daughter, to himself and to his wife. All the others, whether or not they ever actually had the disease, were cured, but these 2 resisted all treatment.

CASE 11—The patient spent a great deal of time catching her "insects" in the bed.<sup>11</sup> When she put them into water she could see them "wiggle", so of course "they were alive."

CASE 12—The patient spent many hours a day rubbing herself with bread crumbs to bring out the insects.

CASE 13—The patient washed and brushed her dog for four days in succession and became "infested" herself with the dog fleas. The insects came about the middle of the day "like a swarm."

CASES 14 and 15—The patients were maiden sisters. One sister became "infested" by sleeping in a bed which had been occupied by a man who had a rare tropical

<sup>9</sup> Perrin, L. Des nevrodermies parasitophobiques, *Ann de dermat & syph* 7 129, 1896

<sup>10</sup> Raecke. Ueber Hypochondrie, *Allg Ztschr f Psychiat* 59 390, 1902

<sup>11</sup> Macnamara, E. D. Note on Cutaneous and Visual Hallucinations in Chronic Hallucinatory Psychosis, *Lancet* 1 807-808 1928



*Cases of Delusion of Parasitosis from the Literature or Previously Unpublished*

Cases No.	Author	Sex	Age	Marital State	Memo at Age	Duration, Years	Type of Sensation Complained of	Where Localized	Kind of Parasite Believed to Be Present	Condition When Last Seen
1	Perrin <sup>9</sup>	F	52		48	2	Pruritus, stinging	General, especially arms, under nails	Unusual kind of flea	
2	Perrin	F	47			$\frac{1}{2}$			Head lice	
3	Perrin	M	46			$\frac{1}{2}$				Same
4	Ruckel <sup>10</sup>	M	36	M		2	Pruritus	Back, arms, legs, genitalia	Scabies mites	Same
5	Myerson <sup>8</sup>	M	40			Several months	Pruritus	Shoulders, back	Insects	Cured
6	Myerson	M	12				Biting, scratching	Generalized	Insects, large and small	Same
7	Glacard <sup>4</sup>	M	40	M		2	Pruritus	Generalized	Itch mites	Same
8	Glacard <sup>5</sup>	F	35	M		2	Pruritus	Generalized	Itch mites	Same
9	Strandberg, (cited by Lkbom)	F	35			Many weeks	Pruritus		Parasites	Same
10	Grøn (cited by Lkbom)	F	65			1	Pruritus	Scalp, neck, back, breasts	Pigeon fleas	Same
11	Macnamara <sup>11</sup>	F	60	S		6	Movements under skin	Generalized	Black winged insects	Same
12	Macnamara	F	61	S		3	Irritation	Scalp and upper part of trunk	Insects, size of flea	Same
13	Macnamara	F	64	M		$\frac{1}{2}$	Irritation, crawling	Face	Dog fleas	Same
14	Macnamara	F	44	S		5	Clicking	Generalized	Small, black things	Same
15	Macnamara	F	42	S		4	Irritation, biting, burrowing	Generalized	Little insects	Same
16	Schwarz <sup>12</sup>	F	57	M		2	Pruritus	Fingers, toes	Poison and insects	Same
17	(Schwarz)	F	33	W	43		Pruritus	Generalized	Lice	Slightly better
18	Schwarz	F	29	M		$\frac{1}{12}$	Pruritus	Generalized	Various kinds of insects	Same
19	Schwarz	F	69			1	Creeping	Generalized	Little brown animals and bacteria	Better
20	Schwarz	F	30			3	Burning, pruritus	Nose, genitalia and generalized	Little insects	Same
21	Flick <sup>13</sup>	M	32				Pruritus	Generalized, especially eyebrows and nostrils	Tiny bugs	Same
22	Mallat and Vale <sup>13</sup>	F	36	M		1	Pruritus stinging	Scalp, breast, back	Public lice	Same
23	Werther <sup>14</sup>	M	40				Pruritus	Generalized	Worms	Same

24	Worth	M	50		Recent	Pruritus	Generalized	Insects	Cured
25	Wilhelm <sup>1</sup>	F	Old	M	5	Pruritus	Generalized	Black, threadlike insects	Same
26	Wilhelm	F		S	8	Pruritus	Scalp	Insects new to science	Same
27	Wilhelm	M			2	Pruritus	Generalized, especially nose	Bacteria	Same
28	Wilhelm	F	50		2	Pruritus	Generalized, pubic	Insects	Same
29	Wilhelm	M	50		2	Pruritus, biting	Generalized, pubic	Insects	Cured
30	Klauder <sup>11</sup>	F	60	M	Recent	Pruritus	Generalized	Chicken mites	Cured
31	Weldner <sup>2</sup>	M			5	Pruritus	Generalized	Dog fleas	Same
32	Weldner	F	50	M		Pruritus	Generalized, especially right leg	Dog fleas	Same
33	Weldner	F				Pruritus	Generalized	Little animals	Same
34	Weldner	M				Pruritus	Generalized, especially scalp	Insects	Same
35	Bleumel <sup>11</sup>	F	50	M	2	Pruritus	Generalized, especially scalp, pubis	Unusual itch mite or tick	Same
36	Bleumel	M	81	W	1/2	Aggravation only	Nails, eyebrows, face	Skin colored insects	Same
37	Bleumel	F	43	M		Pruritus	Shoulders and back	Bedbugs and lice	Worse
38	Ikonom <sup>2</sup>	F	50	M	1/2	Pruritus	Scalp, back, neck and ears	Little insects	Same
39	Ikonom	F	50	M	2	Pruritus	Scalp, mons veneris	Itch mites	Same
40	Ikonom	F	32	W	2	Sticking	Generalized, especially genitalia	Pubic lice	Better
41	Ikonom	F	50	M	1	Pruritus, biting, creeping	Generalized, especially scalp	Little animals	Same
42	Ikonom	F	38	M	1	Pruritus	Chin, scalp, back and arms	Worms	Same
43	Ikonom	F	70	M	2	Pruritus	Right scapular region	Bacilli	Better
44	Ikonom	F	38		1/4	Creeping over skin	Generalized	Little "clothes mite"	Same
45	Ikonom	F	64	S	8	Creeping	Generalized	Worms	Same
46	Miller and Wilson	M	47	S	20	Pruritus, creeping	Generalized, especially face	Lice, new variety	Same
47	Miller and Wilson	F	60	S	1/12	Pruritus	Generalized, especially scalp	Itch mites	Same
48	Miller and Wilson	M	52		1/12	Pruritus	Back of neck	Insects new to science	Same
49	Miller and Wilson	F	51	M	1/2	Digging	Generalized, especially all orifices	Insects	Same
50	Miller and Wilson	F	40	M	1	Pruritus	Generalized, especially ears, vagina and rectum	Insects	Cured
51	Miller and Wilson	F	51	W	11	Pruritus	Generalized	Insects	Same

disease. When she rubbed her body she could hear the insects "clicking." They were tiny and black and looked like powder in the bed. The other sister did not become "infested" until a year later, she described the insects as "tiny black and white insects, as fine as dust, which sprang from the hair into the eyes, ears and nostrils." Both women kept their hair clipped.

CASE 16—The patient had seen her insects with an ocular loupe and was certain of their existence. She stated that poison (as well as insects) was present under her skin. Opium improved her slightly.

CASE 18—This patient stated that "thousands of tiny animals came out of the skin." They could be seen with a lens. The patient, as well as her mother and daughter, had migraine. She was hypertensive. Opium was given to her, and some improvement was noted. Later, however, she stated that even her husband could then see the insects.

CASE 19—This patient no longer slept in a bed, but she lay on a clean cloth on a wooden bench because it was easier to keep it absolutely clean.<sup>12</sup> During her menopause she had had a depressive episode and had attempted suicide. A brother had a war psychosis, and a sister had committed suicide because she believed that she had uterine cancer.

CASE 22—This patient apparently acquired new parasites from time to time, and they appeared first at the tips of her fingers.<sup>13</sup> Then they wandered over her body.

CASE 23—The delusion in this patient was precipitated by the shock of an accident in which his sister lost her vision as the result of his negligence.<sup>14</sup>

CASE 24—The delusion developed in this patient after an incident which occurred while he was in a steam bath. For some reason an attendant had sprayed the air, and the patient believed the spray was employed because insects were present. When the real reason for spraying the air was explained to him, he overcame the delusion.

CASE 26—The patient had auditory hallucinations,<sup>15</sup> claiming she could hear the insects "knocking."

CASES 28 and 29—The patients, man and wife, were both affected. The husband's delusion seemed to have been less well "fixed" than the wife's, as he later denied that he believed in the insects. These insects "spun webs." The wife claimed to have an entire brood under her shoulder blade.

CASE 30—The patient's husband had cleaned out a chicken house, and one of the chickens was said to have been "mangy" and covered with mites. The husband brought the "mites" to her, and "now her children have become infested." She recovered after an analytic discussion of her symptoms.

CASE 31—The insects always jumped on this patient each evening about one hour after he had eaten dinner. They were "light shy," and, although he could

<sup>12</sup> Schwarz, H. Zirkumscribte Hypochondrien, *Monatschr f Psychiat u Neurol* 72 150-164, 1929.

<sup>13</sup> Mallet, R., and Male, P. Delire cenesthetique, *Ann med-psychol* 88 (pt 2), 198, 1930.

<sup>14</sup> Werther, J. Die neurotischen und hysterischen Dermatosen, *Dermat Wchnschr* 96 461-470, 1933.

<sup>15</sup> Wilhelm, J. Ungezieferwahn, *Med Welt* 9 351-352, 1935.

see them dimly in the dark, when he turned on the light they disappeared instantly. He had an elaborate theory to explain why the insects selected him as host. He reasoned that people have poisonous substances in their blood which keep insects away. These poisonous substances are probably derived from tobacco, alcohol, faulty diet, factory work with metals, oils and benzine and similar things. He himself, not having indulged in any of these for twenty-two years and having lived continually in the open air, had a fine, pure blood, hence, insects liked him just as they liked animals. He had had an injury to his right leg thirty-five years previously, and the insects concentrated on this leg ten times as much as on the other.

He also had auditory hallucinations, as he stated that he could hear the "little devils" saying "Here he is, here he is. Come, come, we will warm ourselves, we will warm ourselves."

CASE 35—This patient soaked her head in kerosene every night and morning.<sup>16</sup> She bathed her body at least once a day, after each bath her sister scraped her skin with a knife, and they carefully disposed of the scrapings by burning. She kept the pubic hair shaved and the entire abdomen covered with adhesive tape. She claimed her parasites differed from the common *acarus* of scabies by having male elements at one end and female at the other. She stated that her own mode of treatment had been somewhat successful, the parasites had recently all turned around in their burrows and now directed their backs toward the surface of the skin.

CASE 36—A physician cauterized one of this patient's "lesions" and thereby drove the insects all over his body. They could not be seen because they were the color of the skin. When the patient pulled them off they left fine threads, at the end of which there was a tiny egg.

CASE 37—This patient boiled the entire family wardrobe each night and all the bedclothes each morning. She insisted that the family bathe in gasoline daily and rub with sulfur and lard. She used a hand lens to pick "parasites" from the skin and examine them. She once attempted suicide when she became hysterical at the "sight of two parasites" on the tablecloth.

CASE 38—This patient had syphilis at the age of 40 and received standard treatment for two years. She had had attacks of urticaria frequently over a period of a month and acquired the delusion of parasitosis during this time. She burned her skin with burning wood to kill the parasites. She claimed that the parasites were not visible until after burning. Her 21 year old daughter had dementia precox.

CASE 39—This patient thought that her insects lived principally in her left ear and came out at night to run over her hair, eyes and breasts. They were described as "long and black with a large head."

CASE 40—The patient had cardiac decompensation and hypertension. She stated that she had the "sort of insects one gets from running around with men," which she got "while making a frivolous woman's bed." Whenever she felt a "bite" she quickly dug out the insect with her finger nail. She had seen them plainly, they were white and varied from the size of a grain of sand to that of a flea, and they had a "sucker" at one end. After adequate medical treatment of her cardiac disorder she was not bothered by the insects but still was not certain that they had left her permanently.

<sup>16</sup> Bleumel, C. S. *The Troubled Mind* Baltimore, Williams & Wilkins Company, 1938, pp. 85-87.

CASE 41—This patient had acquired syphilis at the age of 36 and had had five years of treatment. After each visit she was willing to admit that she might have been mistaken about seeing the insects, but she soon returned again with the same story as before.

CASE 42—This patient had hypertension. In addition to the worms which she claimed were embedded deeply in the skin all over her body, she specifically pointed out a tiny nevus on the upper lip in which she stated there was a worm. She also claimed to have a worm in her stomach and could feel it "sucking."

CASE 43—For many years this patient had pruritus limited to the right scapular region, where she had been struck by a man's fist twenty years previously. For the past year only, she had believed that she had parasites at that point. They were too small to see, and "bacteria would probably be a better name, as insects should be visible." After a course of therapy with phenobarbital she said "the insects were more peaceful but had not disappeared."

CASE 44—This patient's parasites lived behind the stove during the day and she could never see them, but at night as soon as she had retired they crept into bed with her to warm themselves. They were so quick that as soon as she turned on the light they were gone. She believed they were "clothes mice," since they gnawed small round holes in the bedclothes. She stated that they "must be some sort of foreign mice to be so small." She had seen them twice, they were coal black and 3 to 4 cm long. She often got out of bed and sat unclothed on a stool to obtain rest. She was placed in a sanatorium for six weeks, during which time she was not bothered by the insects. On her first return visit to her physician she was still "free," but on the second visit she reported that they had come back "one by one" and were "all back at that time."

CASE 45—This disoriented and refractory patient had delusions of grandeur and persecution. She believed she was a princess and demanded a million kronor daily as damages for "false imprisonment." She said her persecutors had injected into her skin worms which they had obtained from a coffin.

#### REPORT OF OUR CASES

We present here an account of 6 cases which have come under our observation. These cases are also recorded in the table.

CASE 46—A C, a single white man aged 47, had been a ship's captain and had spent thirty years at sea. He complained of itching and creeping sensations which involved the face severely, but all other parts of the body had been affected at times. The disorder had begun twenty years previously with a crawling sensation about the genitals and perineal region. He believed pubic lice (*Pediculus pubis* [Phthirus]) to be present at that time but could never find them. He tried strong mercurial ointment, and within a day or so this medication had "driven them all over the body." One of them even got into his eye. Frequently during the past few years he had used a proprietary camphor-phenol compound which he rubbed all over the affected areas. "Five hours later the bugs came out" and he "could pick them off." He was never able to see them move or to see them at all until after this preparation was applied because they "were too deep in the

skin" He also tried tincture of larkspur, but this was not a "good remedy," as it seemed to "get the insects mad," and their "bites" became so severe that he was unable to "stand the pain" The insects were not transmissible, and to his knowledge no one acquired them from him He had periods of comparative freedom as he learned that "when he didn't bother them they did not bother him"

He brought in a piece of gummed cellulose tape with at least a hundred "bugs" stuck between two layers These were all bits of epithelial debris, bits of wool, crusts from healing lesions and blood clots

His skin was clear except for a few excoriated areas and occasional dry scaling areas resulting from overmedication and bathing Physical examination revealed essentially normal conditions

He was shown pediculi, fleas and bedbugs for comparison with his "insects," but he insisted that his parasites were entirely different from any common varieties and that his was the first such case known to science He thought that the insects might have been his own spermatozoa, repressed as a result of continence during long periods of time spent at sea

He was referred to us from the psychiatry department at this hospital, where he had come to be studied for "epilepsy" of two years' duration The story of attacks as he told it suggested a hysterical phenomenon rather than true epilepsy He paced the floor all during the interview and became increasingly nervous as time passed

CASE 47—An unmarried white woman aged 66 was hospitalized after a moderately severe coronary occlusion She was mildly edematous and slightly cyanotic She exhibited several delusions, among which was the conviction that she had become infested with scabies from a patient in an adjoining bed The areas affected by her pruritus, however, bore no resemblance to the usual distribution of scabies, as she complained especially of involvement of the face, scalp and legs She could not see the insects, in fact, she could not "dig them out because they were too deep" The delusion was not constantly present, at intervals she believed that the insects had disappeared One month after the episode began she died suddenly, probably from rupture of the myocardial infarct The delusion had last been discussed on the morning of her death

CASE 48—V B, a man aged 52, had been a scientist of some distinction in previous years and had written several creditable volumes on scientific subjects Now he claimed to have discovered the explanation of numerous widely differing phenomena which appear utterly fantastic

Seven months prior to his first visit to our office there developed on the back of his neck an eruption which he attributed to a hitherto undiscovered insect from Central America and for which he had coined a pseudoscientific name This insect, he claimed, dropped from newly installed lights in the drafting room where he was working He stated that a few years earlier he had a similar infestation which he thought was acquired from handling fresh fruit from Guatemala

The back of his neck was covered with pea-sized to lima bean-sized crusted lesions He constantly dug at the areas in an attempt to remove the "insects" He studied the material removed from the lesions under the microscope and presented a detailed drawing of the insect as well as an illustration of its copulation

He brought suit against his former employers for compensation for the infestation On one occasion he attempted to obtain work at a government agency, and his bizarre actions resulted in his being placed under arrest overnight

Psychiatric consultation resulted in a diagnosis of paranoia, and the psychiatrist flatly stated that the condition was incurable

CASE 49—D C, a woman aged 51, complained of insects digging into her skin for the previous four months Her mouth, throat, eyes and nose were "full of them" Her eyes were almost closed because of edema resulting from her attempts to rub insects out of them The rectum and vagina were also said to be "full of them"

She brought in a collection of lint from black clothing and bits of dried blood, which she believed to be insects She had sterilized all her clothing and bedding numerous times Her skin was dry and crenated from the use of sterilizing solutions She gave away her curtains and rugs because repeated cleaning failed to remove the insects from them

It was impossible to induce the patient to see a psychiatrist Examination by an internist did not reveal anything of interest Her husband is a mental and physical casualty from his attempts to cooperate with her search for a remedy which will destroy the insects She is probably paranoid

CASE 50—F K., a woman aged 46, had been troubled for one year with pruritus caused by "insects" in her skin When first examined she was in bed, sleeping nude on newspapers to catch the parasites Her ears, vagina and rectum were stuffed with toilet paper to keep the insects out The legs of the bed were in pans of cresol solution In spite of all these procedures she stated that the insects crawled up the walls to the ceiling and dropped onto her bed Physical examination revealed nothing abnormal

She was referred to a psychiatrist and was committed to an institution for mental diseases, she returned one year later apparently cured The disease of this patient probably belongs in the involutional melancholia group, as she exhibited a greater fear reaction than is usual

CASE 51—J H, a widow aged 51, is a person of higher than average intelligence When first seen, eleven years previously, she exhibited a severe sulfur dermatitis following successful treatment for a presumptive attack of scabies She returned seven months later with a new "attack", this was due, she believed, to opening a chest brought from the Orient which, she thought, harbored some unusual insect Many pieces of lint were examined microscopically, but no insects were found

She apparently forgot the delusion for a time, but three years later she appeared with another "attack" There was another remission, which in turn was followed by another "attack" three years later, also soon remitting However, two years ago she had another recurrence, which is still present and apparently "fixed"

She sees the insects jump from her daughter's face, and they come down in "doves" to feed on her blankets She has had specimens examined by numerous physicians and parasitologists, but with negative results Every month or two she brings in a new sample of lint, dried blood and similar things Her skin is dry and crenated from the use of disinfectants She spends her entire time from early morning to late at night cleaning, scrubbing and sterilizing her home All available money is spent on cleaner's bills for clothing, bedding, curtains and similar items

It has been impossible to induce her to consult a psychiatrist Physical examination by an internist has not revealed anything of interest She probably has long-standing dementia precox, paranoid type

## COMMENT

"Delusion of parasitosis," in our tabulated series of 51 cases, affected 15 men (29 per cent) and 36 women (71 per cent). Of 31 patients whose marital status is known, 20 (64 per cent) were married, 7 (23 per cent) were single and 4 (13 per cent) were widowed. Of 9 whose age at the menopause is known, in no instance did the delusion occur before it or simultaneously with its onset, the number of years between the development of the menopause and the appearance of the delusion varied from four to twenty-three. None of the patients exhibited the delusion before the age of 30, 4 were 30 to 39, 11 were 40 to 49, 20 were 50 to 59, 7 were 60 to 69, and 1 was in the eighth and 1 in the ninth decade. The duration varied from one month to twenty years, averaging two years and eight months.

The predominant symptom complained of was pruritus, this occurred in 35 patients (69 per cent). Creeping, crawling, movements, biting, scratching, sticking, digging, burning, clicking, irritation and simply aggravation were the other terms used. Some patients exhibited distinct localization of the disorder in previously injured areas or at the site of some other unrelated disease of the skin. The range in types of parasites encountered has been mentioned previously. Only 5 patients (10 per cent) were classed as cured, while the condition of 4 (8 per cent) was ameliorated and that of 42 (82 per cent) was unchanged. The period of observation in some cases was not mentioned or was too short for therapy to have been successful. The prognosis probably was considerably better than these figures indicate. Modern methods available to psychiatrists may be expected to improve the prognosis still further.

## CONCLUSIONS

The term "delusion of parasitosis" is an improvement in nomenclature over "acarophobia."

"Delusion of parasitosis" is a symptom complex which may occur in the toxic psychoses, dementia precox (paranoid type), involutional melancholia and in paranoia-paranoid conditions.

The prognosis is best in the group with toxic psychosis and next best in the group with involutional melancholia, becomes poor in the group with dementia precox and is practically hopeless in the group with paranoia and the paranoid states.

An outline is presented to guide the dermatologist in handling and referring patients of this sort.

The psychiatrist occasionally—the dermatologist rarely—succeeds in curing these patients. The modern electric shock and insulin shock therapy employed by psychiatrists seems likely to improve the prognosis considerably in certain groups.



The case histories of 51 patients are tabulated and additional unusual features are briefed, mostly from the German literature

Included in the table and by more detailed resume are hitherto unpublished cases of our own

Dr Karl Bowman, professor of psychiatry at the University of California Medical School, read and corrected this manuscript in its psychiatric phases

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## ERYSIPELOID SUCCESSFUL TREATMENT WITH PENICILLIN

Report of a Case

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**T**HE BEST treatment of erysipeloid is debatable. Klauder<sup>1</sup> stated "that it is difficult to evaluate different methods of treatment, since in many cases erysipeloid apparently runs a self-limited course and splinting the hand may be the only required treatment." In an experimental study, Klauder and Rule<sup>2</sup> reported a survival of 12.5 per cent of mice treated with a sulfonamide compound after inoculation with *Erysipelothrix rhusiopathiae*, this is surely a limited therapeutic effect of sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine. They also reported that sulfonamide compounds were ineffective in the treatment of patients with erysipeloid.

The opposite view has been expressed by other authors. Schoch and Shelmire<sup>3</sup> and Eckstein<sup>4</sup> reported success with sulfanilamide, Kulchar and Rosenberg<sup>5</sup> cured erysipeloid with sulfathiazole. In the septicemic form with endocarditis, neither sulfanilamide<sup>6</sup> nor sulfathiazole<sup>7</sup> proved to be effective therapeutic agents.

The use of anti-*erysipelo*thrix-rhusiopathiae serum was recommended by Klauder<sup>2</sup> as the treatment of choice for severe forms of erysipeloid but he<sup>1</sup> warned against its use in the commonly encountered type of

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1 Klauder, J. V. Erysipeloid as an Occupational Disease, *J. A. M. A.* **111** 1345-1348 (Oct. 8) 1938.

2 Klauder, J. V., and Rule, A. M. Sulfonamide Compounds in Treatment of *Erysipelothrix Rhusiopathiae* Infections. *Arch. Dermat. & Syph.* **49** 27-32 (Jan.) 1944.

3 Schoch, A. G., and Shelmire, B. Erysipeloid of Rosenbach Successfully Treated with Sulfanilamide, *Arch. Dermat. & Syph.* **41** 570-571 (March) 1940.

4 Eckstein, A. W. Erysipeloid. Report of Case Treated with N-R<sub>1</sub> and Sulfanilamide, *Rhode Island M. J.* **24** 41-45 (March) 1941.

5 Kulchar, G. V., and Rosenberg, E. Sulfathiazole in the Treatment of Erysipeloid. *Arch. Dermat. & Syph.* **43** 846-847 (May) 1941.

6 Russell, W. O., and Lamb, M. E. *Erysipelothrix* Endocarditis. A Complication of Erysipeloid. *J. A. M. A.* **114** 1045-1050 (March 23) 1940.

7 Klauder, J. V., Kramer, D. W., and Nicholas, L. *Erysipelothrix Rhusiopathiae* Septicemia. Diagnosis and Treatment. Report of Fatal Case of Erysipeloid. *J. A. M. A.* **122** 938-943 (July 31) 1943.

erysipeloid because of serum reactions. More recently excellent therapeutic results were reported by Griswold and Bowen,<sup>8</sup> who treated 15 patients with erysipeloid by the local application of solid carbon dioxide.

Since its introduction, penicillin has been tested against most of the recognized pathogenic organisms. Heilman and Herrell<sup>9</sup> experimentally infected 80 mice with *Erysipelothrix rhusiopathiae*, of the 40 mice treated with penicillin, only 2 died, a mortality rate of 5 per cent, all the 40 untreated mice died.

#### REPORT OF CASE

A 23 year old white soldier, a staff sergeant in the Army of the United States, was admitted to the Army Air Forces Regional Station Hospital, Hunter Field, Ga., on Sept 22, 1945. He stated that on September 11, while on furlough, he was crabbing on Lake Pontchartrain, New Orleans, and was bitten on the right thumb by a salt water crab. To effect its removal, the crab's claw had to be broken. No medical treatment was sought. Three days later, on September 14, the right thumb became swollen, red and tender, and movement of the thumb became painful and limited. He bathed his hand in a hot solution of magnesium sulfate and applied a linseed poultice, without benefit. The involvement slowly spread to the dorsum of the hand and the thenar eminence. The man said that he had no elevation of temperature, chill, anorexia or other systemic reaction.

Examination of the right thumb revealed an intense swelling and a diffuse cyanotic erythema. On the radial side of the proximal phalanx was a healing laceration 8 mm in length. The radial third of the dorsum of the hand and the thenar eminence presented several purplish red, irregularly shaped, slightly elevated plaques, measuring 1 to 1.5 cm in diameter. There was no evidence of suppuration or lymphangitis. In the right axilla a solitary lymph node about 2 cm in its longest diameter, was palpable, in the left axilla a smaller node, 0.8 cm, was felt. The remainder of the physical examination revealed no abnormalities.

Reaction to the Kahn test was negative. The urine was normal. The blood count was 4,370,000 erythrocytes, 15.7 Gm of hemoglobin and 4,750 leukocytes with 58 per cent neutrophils, 40 per cent lymphocytes and 2 per cent eosinophils. The blood sedimentation rate (Cutler method) was 14 mm for sixty minutes. A roentgenographic study on the patient's admission to the hospital showed a swelling of the soft tissues of the thumb. There was no evidence of osteomyelitis, necrosis of the bone or periostitis as reported by me<sup>7</sup> previously. On culture the peripheral blood was sterile after ten days' incubation.

With the area under infiltration anesthesia with 4 per cent solution of procaine hydrochloride a bit of tissue was removed from the dorsum of the base of the thumb with a no. 2 Keyes biopsy punch. This specimen was streaked on blood agar plates and Bacto-Sabouraud dextrose agar<sup>10</sup> and was cultured in Bacto-Tryptose phosphate broth,<sup>10</sup> both plain and that enriched by the addition of

<sup>8</sup> Griswold, C. M., and Bowen, S. S. Treatment of Erysipeloid by Cryotherapy. *Arch. Dermat. & Syph.* **49** 348-350 (May) 1944.

<sup>9</sup> Heilman, F. R., and Herrell, W. E. Penicillin in the Treatment of Experimental Infections Due to *Erysipelothrix rhusiopathiae*. *Proc. Staff Meet., Mayo Clin.* **19** 340-345 (June 28) 1944.

<sup>10</sup> Manual of Dehydrated Culture Media and Reagents, ed. 7, Detroit, Mich., Difco Laboratories, 1943.

0.1 cc of sheep cells for every 5 cc of broth. None of the mediums showed any growth after seventeen days' observation.

No local treatment was prescribed, a splint was not applied, and the patient was not cautioned about active or passive movements of the involved digit.

The intramuscular administration of 25,000 units (Oxford) of sodium penicillin every three hours was instituted immediately after the initial laboratory specimens were obtained. At the time of the third injection, six hours after penicillin therapy was commenced, the patient reported complete loss of the feeling of tension in the involved finger, return of normal flexion and extension and less erythema. After twenty-four hours of therapy (200,000 units of penicillin) the rash was definitely less intense in color, after forty-eight hours numerous normal foci appeared in the formerly confluent involvement of the thumb, while several of the satellite plaques on the dorsum of the hand and on the thenar eminence had completely disappeared. After a total of 800,000 units of penicillin was administered, the entire rash disappeared and the patient was discharged to full duty on September 26.

On September 29 the soldier returned to the dermatologic clinic for a follow-up visit. He had no complaints, the right thumb was desquamating but otherwise was normal. The lymph node in the right axilla was now equal in size to that in the left. On October 6 there was no evidence of former disease, the blood count was normal, the blood sedimentation rate was 5 mm for sixty minutes, and the roentgenogram revealed nothing abnormal.

The treatment of erysiploid as described in this paper has certain features that deserve comment. The treatment consisted of intramuscular administration of penicillin alone and no local measures which might account for the cure. Repeated intramuscular injections of penicillin require hospitalization which is not a factor in the army but is an important economic feature in civilian practice. Perhaps this objection will be overcome by penicillin administered orally or by change of dosage. In future cases the optimum dosage should be determined, with the complete subsidence of symptoms after 50,000 units of penicillin. I believe that erysiploid might respond to fewer but larger injections. In this way the treatment may become an office procedure.

It is believed that the failure to culture *Erysipelothrix* from the tissue excised from the lesion does not detract from the validity of the case, both the anamnesis and the eruption were typical of erysiploid.

## Clinical Notes

### LEUKONYCHIA STRIATA SEMILUNARIS

OSWALDO G COSTA, M D, BELLO HORIZONTE, BRAZIL

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Ungual achromia is met with in spots or striae either transverse or longitudinal, and sometimes it covers the whole ungual surface

Spotted and striated leukonychias are common, being characterized by white spots or striae on the nail. Total leukonychia is rare according to Eller and Anderson<sup>1</sup>. In Pardo-Castello's<sup>2</sup> book three more cases are mentioned, 1 reported by Fox,<sup>3</sup> 1 by Stubenbord and Stubenbord<sup>4</sup> and the third by Pardo-Castello himself.

Both partial and total leukonychia may be the result of a diffusion of the lunula. According to Pardo-Castello<sup>2</sup> diffusion of the lunula is common in leprosy and in other dystrophic conditions of the extremities. Greco<sup>5</sup> cited a case in which diffusion of the lunula took place in consequence of therapeutic applications to the ungual matrix. Referring to total leukonychia, Eller and Anderson<sup>1</sup> attributed it to a functional disturbance of the nail matrix producing abnormal keratin formation. This functional disturbance may be due to traumatism, debility, infectious diseases, poisons or neuroses though in some cases none of these factors can be incriminated. Referring to the causal factors of total leukonychia, Stubenbord and Stubenbord<sup>4</sup> affirmed that "the exact etiologic factor is not known, but generally the disorder has occurred in association with conditions such as typhoid, anemia, chronic arthritis with rheumatic endocarditis, measles, multiple neuritis, febrile diseases associated with malnutrition, trophic disorders and trauma."

In my case, by surveying the information given by the patient, the conclusion was arrived at that the lunulae of all the fingers were displaced, retaining clearly their semilunar form and milky color. The displacement of the lunulae took place from the root of the nails toward their respective free edges and occurred slowly, accompanying the growth of the ungual layer. At the same time there was observed a formation of new lunulae at the root of nearly all the nails. Between the displaced lunula and the ungual layer there was a depression shaped like a slight transverse furrow (line of Beau).

<sup>1</sup> Eller, J. J. and Anderson, N. P. Leukonychia Totalis, M. J. & Rec. **127** 318-319 (March 21) 1928.

<sup>2</sup> Pardo-Castello V. Diseases of the Nails, ed. 2, Springfield, Ill., Charles C. Thomas Publisher, 1941, p. 87.

<sup>3</sup> Fox, H., cited by Pardo-Castello<sup>2</sup>.

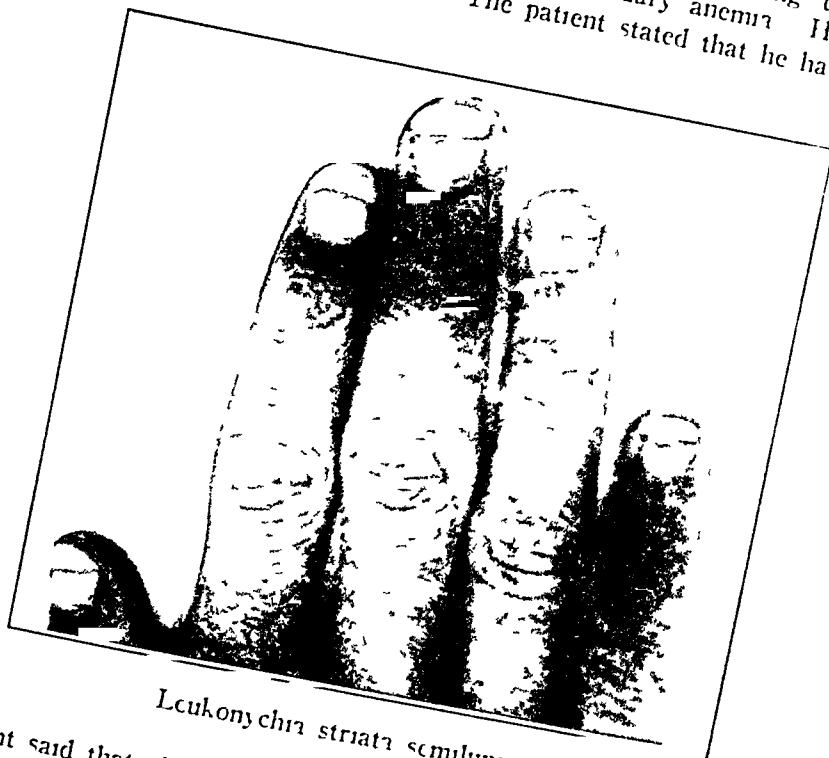
<sup>4</sup> Stubenbord J. G. and Stubenbord, W. D. Leukonychia Totalis, Arch. Dermat. & Syph. **32** 761-763 (Nov.) 1935.

<sup>5</sup> Greco, N. V. Doble lunula ungual temporaria, Semana med. **1** 1718-1720 (June 13) 1935.

A few months previously my patient had had measles and was suffering from anemia due to verminosis. As has been said, Stubenbord and Stubenbord<sup>4</sup> included measles and malnutrition in the causes of leukonychia. In the case of my patient it can be deduced that both the measles and the anemia, together or separately, exercised a predominating action as agents determining the diffusion of the lunulae.

## REPORT OF A CASE

The patient, A. V. T., aged 18, was a Brazilian farm worker, residing at Barra do Cuicé, (State of Minas Geraes). The family history revealed nothing of interest, according to his personal history the patient had had verminosis and secondary anemia. He had measles four months before he consulted me. The patient stated that he had not suffered previous traumatism.



Leukonychia striata semilunaris

The patient said that about four months previously there appeared at the base of his nails dead white spots which in course of time spread toward the free edges. Physical examination showed nothing abnormal except verminosis and secondary anemia.

**Dermatologic Examination**—It was noticed that the whole of the anterior half of each finger nail was completely achromic. Some nails had lunulae, others did not. Between the achromic and the healthy regions of the nails there were slight transverse depressions.

**Laboratory Examination**—The Kahn reaction was negative. The stools contained *Ascaris lumbricoides*.

## SUMMARY

A case is reported of leukonychia striata semilunaris due to diffusion of the lunulae of all the finger nails in a male suffering from verminotic anemia and who had suffered from measles four months previously.

Rua Ceara, 1691

**RATIONAL PHARMACEUTIC TREATMENT OF DISEASES OF THE SKIN**

Keratoplastic Chemicals Become Keratolytic When Prescribed in Fatty '  
Vehicles of High Water Content

HERMAN GOODMAN, M D, NEW YORK

The introduction of high water content vehicles for active ingredients intended for application to the skin in health and in disease requires a revision of ideas as to prescription writing. In former days, salicylic acid, for example, was prescribed in a fat and a fatlike vehicle of hydrous wool fat, petrolatum, theobroma oil, lard, prepared suet or goose grease. These were solid bases. The powdered salicylic acid was dispersed through the art of pharmacy. If the salicylic acid particles were considered as black pawns, an ointment of 10 per cent salicylic acid could be considered as 1 black pawn set among 9 white ones, representing the fat and fatlike ingredients of the vehicle. If the covered skin were then the checkerboard, 1 square in 10 would have salicylic acid, 9 squares in 10 would be covered by grease.

Today, the prescribing physician tends to write for trade name vehicles. He ignores or forgets or is not told the solid content of the vehicle he prescribed. Let it be assumed that the trade-named vehicle has 50 per cent water content. A prescription for 10 parts of salicylic acid in 90 parts of the trade vehicle becomes, in effect, 10 parts of salicylic acid in 45 parts of fat and fatlike solids. Continuing the analogy of black and white pawns on a checkerboard, 2 squares are covered by salicylic acid to 9 covered by the vehicle, since the water evaporates on application and exposure.

Some trade vehicles offered as substitutes for fat and fatlike wool fat, petrolatum, theobroma oil, lard, prepared suet and goose grease have no more than 10 parts of solids to 90 parts of fluid content. A prescription of 10 per cent of salicylic acid in such a vehicle becomes, in effect, a 50 per cent salicylic ointment, as the 10 parts of salicylic acid are matched against 10 parts of combined solids. Half the squares of the checkerboard area are covered by the salicylic acid, rather than 1 in 10 as the prescriber may have intended.

Another example may help. Chrysarobin is prescribed in a medium of chloroform. Review of suggested prescriptions in textbooks, examination of actual prescriptions in pharmacy practice and discussion at staff meetings and on rounds of wards disclose great variation in the percentage of chrysarobin ordered. The evaporation of the chloroform from the skin at the time of application levels all distinction as to percentage of chrysarobin. The film on the skin is 100 per cent chrysarobin.

The knowledge of reduction and oxidation has changed considerably since the late Paul Unna propounded his theories of high and low concentration of the reducing chemicals on the skin with epidermis intact and corium exposed. In practice the ideas advanced by Unna are still applicable. Hence a prescribing physician seeking keratoplastic activity of salicylic acid in less than 6 per cent concentration writes for this active reducing agency as follows:

	Gm. or Cc.
Salicylic acid	4
Zinc oxide	25
Starch	25
Petrolatum enough to make	100

To utilize trade vehicles, the prescribing physician, still seeking keratoplastic activity of salicylic acid in less than 6 per cent concentration writes for this active reducing agency as follows

	Gm or Cc
Salicylic acid	4
Zinc oxide	25
Starch	25
Trade vehicle, enough to make	100

The salicylic acid has automatically been increased in concentration from the keratoplastic less than 6 per cent to the keratolytic greater than 6 per cent because the trade vehicle, containing much water, is only partly solid. The effect on the skin is exactly opposite that sought by the prescribing physician.

#### SUMMARY

Untoward effects from a prescribed low concentration of active reducing agency chemicals (keratoplastic) may be the result of unwitting application of a high concentration of active reducing agency chemicals (keratolytic) in trade vehicles of high fluid content. Prescription writing in dermatologic practice requires consideration of this factor to attain the end results sought by the physician. The composition of each trade vehicle, particularly its content of solid, nonevaporating ingredients, must be known. The quantity of active reducing agency of the chemical ingredient must be compared with the total solid content of the finished preparation on the skin to judge properly the effect so far as keratoplastic or keratolytic action is concerned.

### CUTANEOUS IRIDIFORM GANGRENE DUE TO A CHEMICAL AGENT

OSWALDO G. COSTA, M.D., BELLO HORIZONTE, BRAZIL

Extramural Teacher, Clinic of Skin Diseases and Syphilis, Faculty of Medicine  
University of Minas Geraes

The variety of gangrene here reported on is not of great interest in regard to causation. But my interest was aroused by its clinical form which I believe has never been recorded before as I have found no case similar to mine in medical literature. The name, cutaneous iridiform gangrene, chosen by me was based on similarity between the iridiform lesions of the syphilis found in Negroes and the arrangement of my patient's lesion in concentric and excentric circles.

My patient's skin, which is black, took on a much more intensely black shade which was almost generalized over the body, constituting a true melanoderma brought on by the absorption of mercury.

According to the patient's statement the excentric progress of the gangrene took place as follows. Some days after the application of the mercury salt preferably in the recent peripheral groove a certain part of the skin outside that groove became black and then another groove appeared a short distance from the original one and in this way the gangrene arose.

The treatment consisted in stopping the use of the mercury salt and applying a weak solution of potassium permanganate. At present gangrene no longer exists and the ulcerative process which was extensive is improving steadily. While the mercury salt was being used the patient did not clean the lesion hence the remedy remained at the spot where it was deposited and became mixed with the gangrenous secretion.



## REPORT OF A CASE

H J S, aged 17, a Brazilian rural laborer, was born in the state of Bahia and was living in Bello Horizonte. In the family and personal histories there was nothing abnormal. The patient stated that three months previously he had injured the inner surface of the lower third of the left leg and a small ulcer resulted. He was informed by a friend that mercury bichloride causes rapid cicatrization, and so he bought some at a chemist's to put on his ulcer. After using it he began to notice that the spot where the drug was applied was becoming



Cutaneous iridiform gangrene

black with the edges loose on the underlying tissue. Thinking, however, that the central part was healed while the peripheral zone still continued affected he began the treatment of this zone, with the result that another circular plaque of gangrene was formed. In this way the patient, with his own hands and with the best intentions managed while constantly hoping to cure his ulcer, in the course of time to produce a curious gangrene due to mercury bichloride whose consequences might have been fatal if he had not consulted a physician and received proper treatment.

Physical examination showed nothing abnormal. Dermatologic examination revealed that the patient's skin was much darker than normal, and this was proved by the evolution of the process, for under treatment the skin is gradually acquiring its original color again. Dermatologic examination also showed an extensive plaque of gangrene on the inner surface of the lower third of the left leg, extending to the anterior, internal and part of the external surfaces, this plaque measured 20 by 19 cm. It consisted of six concentric circles, progressing centrifugally and separated one from the other by deep well defined grooves. It had loose edges and a fetid yellowish secretion. The gangrenous skin between one groove and another varied in size from 1.5 to 2 cm. The lesion as a whole presented an iridiform or *en coque* aspect, for the patches of gangrenous skin were separated by deep grooves containing a yellowish secretion. The central part of the lesion was dry. The most pronounced groove was the peripheral one, in which the secretion was abundant. The grooves were all equally well defined, some being more pronounced and others almost obliterated.

The gangrenous plaque was, on the whole, hard on palpation, painless and black. The periphery of the plaque was edematous. There was no acrocyanosis, and before his illness the patient had no subjective symptoms in the left lower limb.

*Laboratory Examination*—There was no glucose in the urine. Wassermann and Kahn reactions were negative. Microscopic examination of the secretion revealed organisms resembling *Corynebacterium diphtheriae*. Cultural examination of the secretion revealed that aforementioned germs were pseudodiphtheric organisms not true *C. diphtheriae*. Inoculation of a guinea pig failed to produce a lesion. No amebas were found. The histopathologic examination was made by Dr. M. Junqueira, who reported the condition as cutaneous gangrene.

Rua Ceará, 1691

## AN UNUSUAL SOURCE OF DERMATITIS DUE TO NAIL POLISH

MAJOR IRVING L. SCHONBERG, MEDICAL CORPS, ARMY OF THE UNITED STATES

Numerous articles have been written on contact dermatitis resulting from the use of nail polish. The following case is of interest because of the unusual source of the dermatitis.

### REPORT OF A CASE

A white woman, 26 years of age, the wife of an officer, came to the dermatologic clinic with a scaly erythematous dermatitis involving the eyelids, sides of the face and anterior portion of the neck. She had been treated by several physicians who had administered roentgen ray therapy and had prescribed various local applications. The location of the lesions suggested a dermatitis due to nail polish, and the patient was advised to discontinue its use. The dermatitis improved shortly afterward with bland local therapy. Several weeks later the patient reappeared with a severe flare-up of the dermatitis on the eyelids, sides of the face and neck. She stated that nail polish had not been used during the preceding two weeks but that the eruption had suddenly recurred two days previously. A patch test with nail polish elicited a strongly positive reaction. A thorough history failed to reveal any other possible allergen. However, on being questioned further she suddenly recalled that nail polish had been used to cover her husband's insignia to prevent tarnishing. In addition, nail polish was used to cover a silver necklace and a silver bracelet, for the same purpose. After the

removal of the nail polish from the insignia, necklace and bracelet, the dermatitis cleared within a week and has not recurred

#### SUMMARY

A case of nail polish dermatitis resulting from the use of nail polish to cover jewelry and insignia is reported

### TREATMENT OF CONDYLOMA ACUMINATUM WITH RESIN OF PODOPHYLLUM

C RUSSELL ANDERSON M D, LOS ANGELES

Culp and Kaplan<sup>1</sup> made a notable contribution to the treatment of condyloma acuminatum with resin of podophyllum. They used a 25 per cent suspension of resin of podophyllum in liquid petrolatum applied with a cotton swab to the surface of the lesions. They found that the growths became blanched in a few hours, appeared necrotic twenty-four to forty-eight hours later, began to slough on the second or third day and promptly disappeared.

I can testify to the efficacy of this treatment. Culp and Kaplan found it impossible to keep the podophyllum suspension confined to the lesions. I have modified their method by using a 10 per cent tincture of Resin of Podophyllum (U S P). This is not an official preparation but is prepared for me by my pharmacist. This is applied to the surface of the lesions with a cotton swab or a camel's-hair brush. Usually only one application is required for cure of the smaller acuminate condylomas. The surrounding normal skin may be protected by an ointment consisting of 25 per cent aluminum powder in paste of zinc oxide (Lassar's paste).

1930 Wilshire Boulevard

1 Culp, O S, and Kaplan, I W. Condylomata Acuminata. Two Hundred Cases Treated with Podophyllin, *Ann Surg* **120** 251-256 (Aug) 1944

### DERMOGRAPHIA, ANOTHER SIDE EFFECT OF PENICILLIN THERAPY

FREDERICK KALZ, M D, MONTREAL, CANADA

Urticaria is one of the few known untoward reactions of penicillin therapy. From May to November 1945 I observed 8 patients in the Royal Victoria Hospital in whom a generalized pruritus occurred after parenteral penicillin treatment and decided dermographia was exhibited. The dermographia started in 3 cases during therapy and in the others from five to thirteen days after the conclusion of therapy and lasted from two to eleven weeks. Five of the patients gave a history of previous eczema, urticaria or hay fever, but none suffered previously from dermographia. No relation to sex, age or an underlying condition was observed in this small group.

In all patients now receiving penicillin therapy, sensitivity to histamine will be determined before and after treatment and the results reported after sufficient material has been collected.

1414 Drummond Street

## A MODIFIED CALAMINE LINIMENT

JOHN G. DOWNING, M.D., BOSTON

One occasionally encounters a patient who has a hypersensitivity to olive oil and therefore gives a reaction to the standard calamine liniment. For several years it has been my custom to use for extremely hypersensitive patients a modified calamine liniment made with heavy liquid petrolatum. In doubtful cases I have prescribed both forms, instructing the patients to use one on one side of the body and the other on the opposite side.

In Boston there has been an extreme shortage of olive oil due to wartime restrictions. It has been necessary, therefore, to use liquid petrolatum. However, considerable difficulty has been experienced by some pharmacists in preparing the mixture. For this reason it is my custom to give the patient a typewritten prescription containing instructions for mixing, as follows:

	Gm or Cc
Prepared calamine N F	80
Zinc oxide	80
Solution of calcium hydroxide	500
Heavy liquid petrolatum	1,000

Place the solution of calcium hydroxide in an electric mixer, and start the motor. Add the calamine and the zinc oxide, and slowly add the heavy liquid petrolatum. Continue the mixing until the product is homogeneous.

Prepared as directed this mixture remains in emulsion for several days. Distilled water can be used instead of solution of calcium hydroxide, and the usual anti-pruritics, such as phenol and menthol, can be added.

## Obituaries

### GIRSCH DAVID ASTRACHAN, M D

1892-1946

Dr Girsch David Astrachan died suddenly on April 30, 1946 of a heart ailment. He was born in Beresina, Government of Minsk, Russia, Jan 4, 1892, and received his early education there. During World War I he was captain in the Imperial Russian Army during 1915 to 1917, becoming a prisoner of war in Germany in 1917 and remaining there until 1920.

He was interested in dermatology at the start of his career, as he became assistant physician in the Municipal Center for Skin and Venereal diseases in Rotterdam, Holland, in 1922. Dr Astrachan graduated from the Thuringische Landesuniversität medizinische, Fakultät, Jena, Germany, in 1923 and came to the United States in 1924. His internship was served at Metropolitan Hospital (1924-1925) under Commissioner Edward M. Bernecker, M D, then superintendent of the hospital.

Dr Astrachan was a member of the American Medical Association, New York Academy of Medicine, American Academy of Dermatology, Society for Investigative Dermatology, Bronx Dermatological Society, Manhattan Dermatologic Society, and Russian Medical Society. He was assistant clinical professor of dermatology at New York Medical College, Flower and Fifth Avenue Hospitals, and associate in dermatology and syphilology, Columbia University. His hospital connections were associate visiting dermatologist, department of correction Hospitals, visiting dermatologist and syphilologist, Metropolitan Hospital, attending dermatologist and syphilologist (outpatient department) Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital. He was a specialist certified by the American Board of Dermatology and Syphilology, Inc.

He wrote and published many medical papers, mostly on syphilis, and completed a number of research and experimental problems. He was a pioneer in the use of oxophenarsine hydrochloride (maphasen), especially in congenital syphilis, and experimented in the use of liver extract for patients who did not tolerate arsenic.

Dr Astrachan was an excellent teacher, loved and respected by his students. Integrity and reliability were foremost among his many admirable qualities. His patients loved him and had the greatest confidence in his ability to help them. Dr Astrachan's life spelled inspi-



GIRSCH DAVID ASTRACHAN, M D  
1892-1946

ration to his colleagues, his family and his numerous friends He was interested in the arts, especially music  
Dr Astrachan married Marie Helen Goldberg, of Granville, N Y, on Jan 3, 1927 He is survived by his wife, his son John and his brothers, Dr Isaac Astrachan of New York, and Lazar Astrachan of Paris, France  
VAN AISTYNE CORNELL, M D

## Correspondence

### IS PENICILLIN A PHOTSENSITIZING AGENT?

*To the Editor* —Under the title "Is Penicillin a Photosensitizing Agent?" Dr Orlando Canizares (ARCH DERMAT & SYPH 52 17 [July] 1945) reports on an interesting case. Since penicillin is such an important drug, the question whether it is also a photosensitizer deserves careful attention, therefore, I should like to comment briefly on Dr Canizares' report.

These are the facts of the case. The patient had taken sulfonamide drugs between January 6 and 19. On January 29 he had received 50,000 units of penicillin. On January 30 he took a sun bath, which was followed by a rather severe erythema. Three days later a morbilliform eruption was noticed at the areas previously most affected by the sunburn.

There is no doubt that one is dealing here with some form of photodermatitis. The question is: Was it caused by the sulfonamide drugs or by the penicillin? One would first think of the sulfonamide drugs because they are known to produce photosensitivity. Dr Canizares has considered this possibility unlikely because of the interval between the discontinuation of the sulfonamide treatment and the appearance of the eruption and because of the fact that the blood did not show residual sulfadiazine prior to the use of the penicillin. However, it is known that small amounts of sulfonamide compounds capable of eliciting allergic reactions may persist especially in the skin long after demonstration of the drug in the blood is possible. I may recall a case (Epstein, S. Studies in Abnormal Human Sensitivity to Light, *J Invest Dermat* 5 187-196 [Aug] 1942 [Case 11, p 193]) of a boy in whom there developed urticaria photogenica following sulfanilamide treatment, which occurred after heavy exposure to the sun three weeks after discontinuation of the drug. This boy, too, had been exposed to the sun between the end of the sulfonamide medication and his first outbreak but less heavily. It seems, in the light of present knowledge, more likely to ascribe the severe reaction after sunburn in Dr Canizares' case to the sulfonamide compounds.

The morbilliform eruption noticed four days after the sunburn and appearing especially in the area most severely affected by the sunburn probably is something different. Photosensitivity covers a lot of different phenomena. One may distinguish manifestations caused by true photosensitizing agents, which may act by primary phototoxicity and/or photoallergy. On the other hand, there is a phenomenon called "phototraumatism." This term covers those eruptions that occur at the site of previous reactions to light. It is well known that dermatophytid or lichen planus or psoriasis may occur exactly at the site of the previously sunburned area. In this instance it is not necessary for the agent that causes the eruption to be a photosensitizer. I recall a patient of mine who had a mild papular dermatitis seven days after injection of tetanus antitoxin (horse serum), the eruption was confined entirely to the area that had been sunburned the day after the serum had been injected. In these cases one may assume that vascular changes in the sunburned area favored the development of local sensitivity of these regions.

The morbilliform eruption in Dr Canizares' case might be explained on this nonspecific basis. All in all, his case does not seem to present sufficient evidence to prove that penicillin is a photosensitizing agent.

STEPHAN EPSTEIN, M.D., Marshfield, Wis.

## PASSIVE IMMUNIZATION OF PEMPHIGUS VULGARIS

*To the Editor* —Drs Arthur W Grace and Leon D Hellman published a paper (Pemphigus Vulgaris Successful Results Following Transfusion with Blood from Persons Who Had Recovered from the Disease, *ARCH DERMAT & SYPH* 53 249 [March] 1946) which implies that this method is a new and original one. As early as 1936 L Kumer (in discussion on Urbach E Versuche einer aktiven Immunisierung von Pemphiguserkrankungen, *Zentralbl f Haut- u Geschlechtsk* 52 277, 1936) reported some astonishing results with injection of blood or blood serum from persons convalescent from pemphigus into patients with this disease. Similar experiences were described by me (same reference). Since convalescent blood or serum is difficult to obtain, I introduced the transfusion of immune serum from rabbits which had been experimentally infected with pemphigus virus and had recovered from this disease (Urbach, E, and Wolfram, S *ARCH DERMAT & SYPH* 33 788 [May] 1936). Since repeated injection of animal serum is liable to induce anaphylaxis, we are now trying the use of despeciated pemphigus rabbit serum.

In passing I should like to call attention to our attempts actively to immunize patients with pemphigus with formaldehyde-treated brain tissues of pemphigus-infected rabbits after these patients had recovered temporarily through the use of passive immunization methods.

ERICH URBACH, M D, Philadelphia

136 South Sixteenth Street

## BENADRYL IN CHRONIC URTICARIA

*To the Editor* —Six patients with chronic urticaria under treatment with Benadryl complained that the medication made them so sleepy that it was not practical for them to use it except at bedtime. All were instructed to take half of a 10 mg tablet of amphetamine sulfate (Benzedrine) at the same time as the Benadryl. All except 1 patient reported complete relief of the annoying drowsiness, and this one was relieved by taking three-fourths of an amphetamine sulfate tablet. The undesirability of prolonged habitual use of amphetamine sulfate is recognized, but these patients required only one or two doses a day, which seems reasonably safe and at least preferable to the obvious alternatives.

HARRY L. ARNOLD JR, M D, Honolulu, Hawaii

## News and Comment

## GENERAL NEWS

**The Society for Investigative Dermatology** —The Society for Investigative Dermatology will resume its annual meetings and is meeting this year at the Hotel Whitcomb, San Francisco, on June 30. The two scientific sessions, from 10 a m to 1 p m, and from 2 to 6 p m, are open meetings and not limited to members only. The scientific program consists of fifteen papers.

**Membership in Philadelphia Dermatological Society** —Election to active membership in the Philadelphia Dermatological Society shall hereafter be restricted to specialists certified by the American Board of Dermatology and Syphilology.

## DEATHS

Dr Mihran B Parounagian died on June 12, 1946.



# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

ALLERGY AS A FACTOR IN SURFACE ULCERS, VARICOSE VEINS, PHLEBITIS AND THROMBOSIS JOHN A TURNBULL, Am J Digest Dis **12** 272 (Aug) 1945

Turnbull reports 6 cases, including 2 of pruritus and eczema and 3 of varicose ulcers of the legs. Successful treatment was based on diets avoiding foods demonstrated by cutaneous tests to be allergenic. Turnbull believes that allergenic foods and other substances may produce inflammation and other reactions in the endothelium of the blood vessels, in the same way that they produce the more familiar sensitizations of the epithelium.

THE USE OF PENICILLIN IN TOPICAL APPLICATION LAWRENCE H SOPHIAN, Am J M Sc **208** 577 (Nov) 1944

Sophian and Connolly performed experiments which showed that in a suitable ointment base penicillin when applied topically has a considerable ability to penetrate a solid agar culture medium, and that penetration is enhanced by the addition of a wetting agent (Aerosol M A). Other in vitro experiments showed that diffusion through the skin is certainly too small for therapeutic utility. Clinical use of penicillin-Aerosol vanishing cream ointment was made in 11 cases and had strikingly effective value in the treatment of acute and chronic pyogenic infections of the skin and subcutaneous tissues, particularly sycosis barbae, infected superficial wounds and furunculosis. The author points out that there are many bacteria which are resistant to low concentrations of penicillin but which are susceptible at higher levels. Chancroid is an example of such a disease, in 1 case excellent results were obtained in seven days.

PENICILLIN WITH SPECIAL REFERENCE TO ITS USE IN INFECTIONS COMPLICATING DIABETES FRANKLIN B PECK, Am J M Sc **208** 581 (Nov) 1944

In a discussion of cellulitis and carbuncles occurring in diabetic persons, Peck points out that penicillin is an invaluable adjunct to treatment. His experience suggests that it may be more effective if given locally directly into infected tissues than if injected parenterally for systemic effect. The solutions used for this purpose ranged from 100 to 1,000 units per cubic centimeter of isotonic solution of sodium chloride.

A CASE OF ECZEMA AS A SOURCE OF A STREPTOCOCCAL EPIDEMIC G K DEFORD and LORRAINE M KERR, Am J M Sc **209** 752 (June) 1945

DeFord and Kerr report a small epidemic of streptococcal diseases among student nurses taking care of a child with secondarily infected eczema. During a three-month period 50 per cent of the nurses who cared for this child became ill with sore throat or scarlet fever.

ALBRIGHT'S SYNDROME (POLYOSTOTIC FIBROUS DYSPLASIA WITH CUTANEOUS PIGMENTATION IN BOTH SEXES AND GONADAL DYSFUNCTION IN FEMALES) MALCOMB B DOCKERTY, RALPH K GHORMLEY, ROGER L J KENNEDY and DAVID G PUGH, Arch Int Med **75** 357 (June) 1945

Dockerty and his associates report 6 new cases of Albright's syndrome. In the course of a thorough general discussion they state that extensive cutaneous pigmentation, often occurring in the form of large irregular patches, is an almost

constant accompaniment of osseous lesions of pronounced degree in Albright's syndrome. These patches of pigmentation may occur with a predilection for the side of the body that has the most pronounced bony lesions. The back, buttocks, inner aspects of the thighs, neck and scalp are common sites. In 1 case a large pigmented spot on the scalp was the only discolored area and was associated with alopecia.

In dermatologic discussions there has been a tendency to question whether this syndrome may be related to neurofibromatosis, but the authors state that the diseases can be distinguished by the fact that neurofibromas do not occur in connection with Albright's syndrome.

EXPERIMENTAL REPRODUCTION OF MADUROMYCOTIC LESIONS IN RABBITS  
DOUGLAS SYMMERS, Arch Path **39** 358 (June) 1945

Symmers reports success in experimental studies with subcutaneous injections of *Phialophora jeanselmei* into rabbits, producing solitary nonulcerative nodules which histologically are specific and are closely comparable to the nodules in that form of maduromycosis in man which is caused by the same fungus.

PHIALOPHORA JEANSELMEI COMB N FROM MYCETOMA OF THE HAND C W  
EMMONS, Arch Path **39** 364 (June) 1945

Emmons describes the mycologic characteristics of a fungus isolated from a patient with mycetoma of the hand which developed after an injury in which splinters from a wooden floor pierced the skin. The fungus resembles *Phialophora*, which is known to occur on wood.

LYNCH, St Paul

MULTIPLE MALIGNANT HEMANGIO-ENDOTHELIOMA IN INFANT REPORT OF CASE  
A R SCHWARTZ, Arch Pediat **62** 1 (Jan) 1945

The author reports a case of multiple malignant hemangio-endothelioma in a 6 week old girl, with the history of emaciation, malaise, poor appetite and progressive swelling of abdomen since birth. On examination numerous hemangiomas scattered over the body and extremities were noted. The abdomen was noticeably enlarged, and the liver extended to the umbilicus. There was severe anemia. The course of the disease was rapid and fatal. Schwartz feels that this case fulfils most of the criteria which were formulated by Kunstader after reviewing 15 cases. The criteria are (1) enlarged abdomen since birth, (2) various gastrointestinal disturbances, (3) progressive course, (4) respiratory embarrassment and (5) anemia.

The clinical course of malignant vascular tumors varies considerably depending on the type present. There are three different types: those with metastasizing hemangiomas running a benign course, in which the health of the child is relatively unaffected; those in which there is a more fulminating clinical course, with rapid loss of weight and cachexia, progressing rapidly, with death in weeks or months; and those which simulate melanotic sarcoma. At necropsy tumor nodules were observed in the middle lobe of the right lung and throughout the liver. There was no histologic evidence of a malignant process.

CETYL TRIMETHYL AMMONIUM BROMIDE IN THE TREATMENT OF A FEW SKIN-  
LESIONS, PARTICULARLY IMPETIGO JOHN A TOOMEY, PAUL M KOHN and  
RALPH C LOHREY, Arch Pediat **62** 108 (March) 1945

Cetamium (cetyl trimethyl ammonium bromide), a quaternary ammonium compound, is an efficient wetting agent, cationic detergent and antiseptic. It can be used for several purposes: to remove dirt and grease, to make surfaces sterile and to remove scabs and crusts from impetiginous areas. It was found to be of value for patients with impetigo who were actually in a hospital or an institution at the time treatment was administered. The treatment was carried out by one or

two persons who were instructed to cleanse the lesions with hot saline solution or solution of boric acid twice daily and apply the cetamium mud (paste) directly to the lesion as a plaster. The material is valueless if cursorily placed over an impetiginous lesion, as it will cake and pus may collect under the crust. In the few cases of resistant impetigo there was clearing after sulfathiazole ointment was used. The authors do not recommend the use of cetamium for cutaneous diseases when caking would be a disadvantage. They thought that the drug was of some value against severe ringworm infections.

GELBER, Los Angeles

EFFECT OF TOPICAL APPLICATION OF VITAMINS AND SOME OTHER CHEMICALS ON THE HEALING OF WOUNDS GROSVENOR W BISSELL, *Arch Surg* **49** 225 (Oct) 1944

Recognizing the general growth-promoting properties of the vitamins, the author studied the effects of various substances when applied directly to wounds. Topical applications were made on wounds of uniform size in normal rats. The substances studied were vitamins A, C, D and E, thiamine hydrochloride, nicotinic acid, riboflavin and other preparations. No definite benefit was derived from the use of any of these substances.

KAISER, Rochester, N Y [*Am J Dis Child*]

THE NEOPLASTIC POTENTIALITIES OF MOUSE EMBRYO TISSUES I THE FINDINGS WITH SKIN OF C STRAIN EMBRYOS TRANSPLANTED TO ADULT ANIMALS II CONTRIBUTORY EXPERIMENTS, RESULTS WITH THE SKIN OF C 3H AND WEBSTER-SWISS EMBRYOS, GENERAL CONSIDERATIONS PEYTON ROUS and WILLIAM E SMITH, *J Exper Med* **81** 597 and 621 (June) 1945

Smith and Rous discuss the results of experimental studies which attempted to test whether embryo epidermis is capable of undergoing neoplastic change. The work showed that epidermal tumors arise with great rapidity and regularity from embryo skin transplanted to adults of a certain homologous strain together with methylcholanthrene. Further studies gave no ground for the supposition that embryo skin has any special liability to neoplastic change, nor did such studies make it possible to assume that the neoplastic potentialities of the transplanted tissues were due to viruses or other specialized precursor agents which are known today.

The authors conclude that the rarity of neoplasms at birth is due to the circumstances of intrauterine life and to its brevity, not to any lack of capacity of the cells of the embryo to undergo neoplastic change.

LYNCH, St Paul

HORMONAL TREATMENT OF ACNE E SIMON, *Union med du Canada* **74** 37 (Jan) 1945

The author cites the following facts in support of the belief that acne is a hormonal disease: 1 It never appears in castrated males. 2 It appears in adolescence and tends to disappear in adult life, when the hormonal equilibrium is reestablished. 3 It develops in females treated with testosterone. 4 It is worse before the menstrual period, when the amount of folliculin in the blood is at its lowest level.

The author thinks that androgenic hormones are acnegenic and that estrogenic hormones protect against the disease. The possibility of anterior pituitary stimulation is discussed, but Simon concludes that as yet such attempts have been unsuccessful in the treatment of gonadal insufficiency or disequilibrium. He prefers to administer diethylstilbestrol (0.5 to 1.5 mg daily by mouth) over a period of at least six months. The possible dangers of such treatment are pointed out, such as feminization and testicular atrophy in males and menstrual upsets in females (metrorrhagia or amenorrhea).

Two cases of successfully treated acne vulgaris are reported.

LAYMON, Minneapolis

THE RELATIONSHIP OF ACNE WITH DANDRUFF AND SEBORRHOEIC DERMATITIS  
E LIPMAN COHEN, Brit J Dermat **57** 45 (March-April) 1945

In an examination of 500 young women, the author noted the amount of dandruff of the scalp and made a search for seborrheic dermatitis. His conclusions are (1) that the association of acne and gross dandruff is supported, and (2) that no support is found for the statement that acne and seborrheic dermatitis are apt to occur together.

PSYCHOGENIC FACTORS IN ACNE E LIPMAN COHEN, Brit J Dermat **57** 48  
(March-April) 1945

The author interviewed a group of men and women with acne. A considerable number of possibly relevant psychogenic manifestations were found, especially among the men and among the higher age groups. The results being uncontrolled, their interpretation is uncertain. Slight evidence was found for a period of strain or fatigue preceding the acne. The clinical impression remains strong that women in the thirties with acne are neurotic.

MULTIPLE SUPERFICIAL CARCINOMATA OF THE SKIN MARY JOHNSON, Brit J Dermat **57** 58 (March-April) 1945

The author reports 5 cases of multiple superficial carcinomas of the skin. The type of lesion appearing on exposed parts, such as the face, differs clinically from that on the trunk. The former is the well known rodent ulcer, which progresses comparatively rapidly, with ulceration and destruction of tissue, the latter is less easy to diagnose unless the miniature rolled edge is recognized, and ulceration in these cases is rare. Lesions of the latter type tend to occur at a younger age and, apart from cosmetic considerations, cause no inconvenience.

A CASE OF ERYTHEMA ANNULARE CENTRIFUGUM G A G PETERKIN, Brit J Dermat **57** 65 (March-April) 1945

The author reports a case of erythema annulare centrifugum that responded dramatically to sulfathiazole.

BLUEFARB, Chicago

CUTANEOUS ANTHRAX TREATED WITH PENICILLIN A M ABRAHAMS, Brit M J **1** 771 (June 2) 1945

A patient with cutaneous anthrax was successfully treated with a total of 600,000 units of penicillin over a five day period. The temperature became normal after twenty-four hours, and the patient was discharged sixteen days after the onset of his illness.

DARK-ADAPTATION STUDIES IN SKIN DISEASE ARTHUR PORTER and E W GODDING, Brit M J **1** 840 (June 16) 1945

A group of patients under treatment for cutaneous disease and a control group numbering about 100 each were tested with the dark adaptation test. There was no significant difference between the mean threshold values of the two groups.

SHAW, Chattanooga, Tenn

SULFONAMIDES IN SKIN DISEASES S L KALLIANPURKAR, Indian J Ven Dis **10** 34 (April-June) 1944

The author recommends sulfathiazole internally (2 to 3 Gm daily) and externally as a dusting powder in treatment of intertrigo. Sulfathiazole orally and a 20 per cent aqueous solution of gentian violet medicinal are advised for infectious eczematoid dermatitis. For ordinary impetigo sulfathiazole is used internally and externally. The author states that alopecia in persons 20 to 30 years of age is often due to acne necrotica miliaris, an opinion with which few dermatol-

ogists will agree. Sycosis barbae, Bockhardt's impetigo and bacterid or allergic dermatitis caused by "a septic focus somewhere" are among other dermatoses for which he advocates treatment with sulfonamide compounds internally and externally.

Lupus erythematosus, erythema nodosum and erythema induratum are diseases which, in the author's opinion, are due to a toxin of tuberculous, nontuberculous or unknown origin. Sulfonamide drugs are advised for these conditions, either parenterally or by external application. Three to 4 Gm of the drug daily for four or five days is said to have favorable results against the organisms.

ARIBOFLAVINOSIS IN NORTHERN PFRU K VIGORS EARLE, J Trop Med & Hyg  
48 10 (Feb-March) 1945

The author surveys the incidence of ariboflavinosis in 403 patients who were hospitalized for all types of disease or accident. The results were as follows: Of patients found to have oral lesions, angular stomatitis occurred in 8.19 per cent, and lingual alterations were present in 3.25 per cent. Of patients suffering from dermal lesions, nasolabial "seborrhea" was present in 16.62 per cent, "seborrhea" of the ears in 3.72 per cent and facial comedos in 26.57 per cent. Oral lesions were far commoner in females, while dermal lesions were more frequent in males.

LAYMON, Minneapolis

A STUDY OF DISEASES OF AUSTRALIAN NATIVES IN THE NORTHERN TERRITORY  
RAYMOND T BINNS, M J Australia 1 421 (April 28) 1945

Diseases which are usually found among the natives but rarely among the white population in Australia are yaws, ankylostomiasis, granuloma inguinale and leprosy. In a study of approximately 400 patients, mostly full-blooded aborigines, 48 per cent had a positive Kline precipitation reaction of the blood. Thirty of the 193 patients who reacted to the test had lesions which were regarded as typical of yaws, and 51 had lesions which resembled yaws, but which could not be described as typical. It may be reasonably assumed that the majority of the remaining 113 reactors to the Kline test (with the exclusion of the occasional positive result which may have been caused by malaria or leprosy) had had a previous spirochetal infection. Yaws responds rapidly to treatment with penicillin. Several persons with gangosa were seen, in all the Kline test produced a reaction. Bony lesions that were regarded as being caused by yaws were frequently seen, and 15 cases of "boomerang legs" with anterior bowing of the tibia were observed. A patient with interstitial keratitis was noted and also a patient with symptoms closely resembling tabes dorsalis.

The important difference between syphilis and yaws, if they are separate entities, is that one predominantly affects the white population and the other the native population. The difference in the mode of living is probably one of the important etiologic factors. The absence of the primary and secondary clinical manifestations of syphilis supports the theory that a widespread infection by *Treponema pertenue* immunized the native population against syphilis.

Twenty patients suffering from granuloma inguinale were seen. They responded well to injections of antimony preparations. Twelve natives suffering from leprosy were found.

HENSCHEL, Denver

CLINICAL TUBERCULIN DIAGNOSTIC BY MEANS OF WEAK INTRACUTANEOUS DOSES,  
WITH SPECIAL REGARD TO TUBERCULOUS SKIN DISEASES P BONNFVIE and  
R BJORNSTAD, Acta dermat-venereol 21 9 (Feb) 1940

There appears to exist large variations in the reactivity against weaker doses of tuberculin (in dilutions down to 0.000001 mg). These variations seem to be strongly dependent on the character of the tuberculous infection and are consequently of diagnostic value. The result of an examination with the aid of graduated intracutaneous tuberculin tests is best judged by the so-called threshold value.

being used as a basis, the weakest dose eliciting a positive reaction. An experimental survey was made on patients with established diagnoses of cutaneous tuberculosis or tuberculids, i. e., lupus vulgaris, tuberculosis verrucosa cutis, ulcerative tuberculosis of the skin, colliquative tuberculosis, acneform tuberculids and erythema induratum. The control material was composed of all patients with positive reactions to the tuberculin tests with nontuberculous diseases of the skin and 85 healthy nurses, a total of 835 persons.

The majority of patients with lupus vulgaris had positive reactions to tuberculin tests with 0.001 mg. or less, with the greatest percentage showing positive reactions to tests with 0.000001 mg. of old tuberculin. Whenever sensitivity to tuberculin was lower than to 0.001 mg. of old tuberculin there was a predominant amount of accompanying pulmonary tuberculosis, demonstrating that sensitivity to tuberculin is reduced by the coexistence of pulmonary tuberculosis. In the same series it was found that sensitivity to tuberculin was reduced with clinical cure of the disease.

In the cases of tuberculosis verrucosa cutis and ulcerative and colliquative tuberculosis of the skin, the threshold in the majority of cases was with quantities of 0.001 mg. of old tuberculin. Among the cases of tuberculids the patient's sensitivity to tuberculin was extremely high. No patient showed a threshold with concentrations greater than 0.001 mg., and 70 per cent of these gave positive reactions to the tuberculin tests with 0.000001 mg. of old tuberculin or less. Slightly lower values were present in the cases of erythema induratum.

Tests of the same type were made on patients with diseases of the skin for which a tuberculous cause had been suspected—namely, lupus erythematosus, Boeck's sarcoid, tuberculosis miliaris disseminata faciei, granuloma annulare and erythema nodosum. Erythema nodosum in tuberculous primary infection in adults showed at first a threshold of 0.1 mg. to 0.01 mg., but in the subsequent months the threshold of sensitivity rose to 0.0001 to 0.000001 mg. of old tuberculin. In cases of lupus erythematosus the patients had a low sensitivity, and 2 did not react to 1 mg. of old tuberculin. Sixteen patients in 45 cases of tuberculosis miliaris reacted negatively to the tuberculin tests, with the highest threshold of 0.01 mg. The sensitivity to tuberculin in cases of granuloma annulare and Boeck's sarcoid was equally low. The authors express the belief that in the absence of tuberculosis of the inner organs a high degree of sensitivity to old tuberculin in amounts of 0.001 mg. or less is indicative of a tuberculous origin of the dermatosis in question.

GENERALIZED HERPES ZOSTER AND LYMPHATIC LEUKEMIA. B. BAFVERSTEDT, *Acta dermat-venereol.* 21:60 (Feb.) 1940.

Hemorrhagic herpes zoster with necrosis and accompanied with a generalized varicelliform eruption appeared in a man 70 years of age. During the course of a routine examination he was found to have a coexisting lymphatic leukemia. Since it is known that a generalized varicelliform eruption occurs in lymphatic leukemia from two to three years after the onset of the disease, Bafverstedt is of the opinion that the eruption was an early symptom of the leukemia. He concludes that in all cases of herpes zoster, particularly of the generalized form, a thorough search for possible blood dyscrasias should be made. On the other hand, he suggests that physicians should watch patients recovering from herpes zoster for some time to avoid the mistake of erroneously diagnosing a transitory lymphatic reaction as true leukemia.

ROBINSON, Washington, D. C.

# Society Transactions

## NEW ENGLAND DERMATOLOGICAL SOCIETY

Jacob H Swartz, M D , *President*

Francis M Thurmon, M D , *Secretary*

*Dec 13, 1944*

**Keratosis Follicularis** Presented by MAJOR EARL A GLICKLICH, M C , A U S

G K , a white man aged 29, presents a generalized pruritic dermatitis of two years' duration, which developed while he was serving in the European Theater of Operations. The diagnosis was confirmed by biopsies at an overseas base hospital. Since the eruption did not respond to therapy, the patient was evacuated and admitted to the Lovell General Hospital on Nov 27, 1944.

Results of physical examination were within normal limits except the eruption, which is generalized. The lesions are discrete, small, firm papules of light, waxy, brownish color at the pilosebaceous orifices. On the anterior portion of the chest, the eruption tends to be confluent and forms an erythematous area which is slightly moist. In the genitocrural region, a mild vegetative tendency is noted.

Results of blood counts, urine tests and roentgen ray examination of the chest were within normal limits. Histologic sections were consistent with the diagnosis of keratosis follicularis.

### DISCUSSION

DR JACOB H SWARTZ, Boston. I do not believe that this is keratosis follicularis. I offer a diagnosis of pityriasis rubra pilaris because of the follicular enlargement on the dorsal aspect of the proximal phalanges, because this eruption appeared only two years ago rather than early in life and because of the involvement of the soles in this case. I did not see the slide. I understand that Dr Lever saw it.

DR WALTER F LEVER, Boston. There was one section that seemed to be consistent with a diagnosis of keratosis follicularis. A lacuna was present, and there were dyskeratotic changes in the lower layers of the epidermis. I was much interested to find small keratotic lesions on the soles of this patient. Such lesions have been described in keratosis follicularis.

DR FRANCIS P MCCARTHY, Boston. I saw the slide. I did not observe the lesions on the sole. I favor the diagnosis of keratosis follicularis.

DR LEONARD E ANDERSON, Springfield, Mass. I thought that the eruption showed the characteristic clinical picture of keratosis follicularis.

DR G MARSHALL CRAWFORD, Brookline, Mass. I do not recall seeing pityriasis rubra pilaris of the scalp. I agree with the diagnosis of keratosis follicularis.

DR JACOB H SWARTZ, Boston. The scalp is involved, sometimes extensively. The eruptions in the cases I have seen, 1 in particular at the Massachusetts General Hospital, have been called psoriasis. That patient was a young girl with rheumatoid arthritis which turned out to be a typical case of pityriasis rubra pilaris with involvement of the soles, palms and scalp.

DR C GUY LANE, Boston. I want to thank Major Glicklich for bringing these cases, and I hope that this will encourage him to bring more.

**Lichen Planus** Presented by MAJOR EARL A GLICKLICH, M C , A U S

The following 3 cases of lichen planus are presented as representative of this disease occurring among servicemen in the Southwest Pacific.

In C D , a white man aged 36, a dry, scaling eruption developed on the lips and eyelids in August 1944. Shortly thereafter, pruritic, raised lesions appeared

on the wrist, dorsa of the hands, forearms, feet and genitalia. Itching was sufficiently severe to interfere with his work and sleep. He was hospitalized overseas September 8. On October 20 he was admitted to the Lovell General Hospital.

Examination reveals a hypertrophic, dry, scaling violaceous eruption which is generalized but most pronounced on the dorsa of the hands, the eyelids and the ears. Lesions typical of lichen planus are present on the buccal mucosa.

Laboratory studies, including blood counts and urinalyses, were normal. Roentgen ray examination of the chest revealed a slight thickening of the right apical pleura. Reactions to serologic tests for syphilis were negative.

In a white man aged 22, vesicular lesions developed between the toes in April 1944. Soon thereafter lesions appeared on the legs, hands and trunk. On June 14, he was hospitalized overseas, and, as the eruption failed to respond to local therapy, he was evacuated and admitted to the Lovell General Hospital on Oct 16, 1944.

Examination reveals a dry, scaling, papular, violaceous eruption on the dorsa of the hands, anterior aspects of the legs and upper portion of the trunk. Results of a general physical examination are normal except for the eruption.

The blood count, urinalyses and roentgenologic studies of the chest were within normal limits. Histologic sections were consistent with lichen planus. Serologic reactions for syphilis were negative.

In a white man aged 30 a pruritic vesicular eruption developed between the fingers and toes in June 1944. Shortly thereafter lesions appeared on the legs, thighs, groin, abdomen, back and face, especially around the eyes and ears. The eruption failed to respond to therapy, and the patient was evacuated and admitted to the Lovell General Hospital on October 20.

The results of a superficial physical examination with the exception of the eruption are within normal limits. The patient presents a generalized violaceous papular, slightly scaling eruption on the hands, feet, trunk and face, involving particularly the eyelids and ears. Small papular lesions resembling leukoplakia are present on the buccal mucosa.

Results of blood counts, urinalyses and roentgen ray examination of the chest were within normal limits. The serologic reaction for syphilis was negative.

#### DISCUSSION

MAJOR EARL A. GLICKLICH, M C, A U S. In the military service this unusual atypical form of lichen planus has been seen for some time. Patients have been returning from the Southwest Pacific Area, primarily from New Guinea. There are a number of these patients invalided back to the United States so that if they have not been seen they will be shortly. What the cause of the eruption is no one knows. An eminent dermatologist recently returned from England and is carrying out a survey of the group in this country. At the present time, another eminent dermatologist from New York city is in the Southwest Pacific Area, where he is studying the dermatologic cases which have been received from that area.

What has been seen today is an atypical type of lichen planus. However, cases have occurred in which generalized exfoliative dermatitis has followed the onset of lichen planus. Some of the patients have had suppression of the bone marrow and aplastic anemia has developed, others have died. There have been other pathologic changes in the body. I offer no explanation. I thought that there might be something to suggest the cause.

DR C. GUY LANE, Boston. It is interesting to hear of such a large group of patients with lichen planus coming from one locality. It again raises the question of the possibility of a bacteriologic or possibly a filtrable virus as the etiologic factor. This recalls the report of Jacob and Helmbold (Jacob, F. M., and Helmbold, T. R. Bacteriologic Studies on Lichen Planus. A Preliminary Report, *ARCH. DERMAT. & SYPH.* 27:472 [March] 1933) wherein they report the isolation of gram-negative anaerobic bacilli from 25 to 28 patients with lichen planus, using a semisolid dextrose-serum agar medium containing cubes of human tissue.



Their study has not been confirmed so far as I know, at least Portma's investigation (Portma, C Experiments in the Culture of the Organism of Lichen Planus by Jacob and Helmbold's Method, *ARCH DERMAT & SYPH* 36 836 [Oct] 1937) failed to yield the organisms described by Jacob and Helmbold. That lichen planus is probably caused by a filtrable virus is an opinion expressed by many dermatologists was stated by Wise and Sulzberger in 1938 (Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1938, p 497). However, such reports certainly raise the question concerning the need for further studies on the possible infectious character of lichen planus.

It is interesting to see the variation in the type of cases which are shown today. The eruption in these 3 cases are fairly well generalized. C D showed considerable pigmentation, especially of the face. He recalls a patient who was seen at the Massachusetts General Hospital some years ago, an Italian who had profuse eruption on both cheeks. Later, there was a good deal of questioning at these meetings as to whether or not that had been lupus erythematosus or lichen planus. If I had not seen it in the beginning and if I had not seen the lesions characteristic of lichen planus, I should have had some doubt. The hands of patient C D showed a good deal of atrophy. I think that the eruption will be permanent. I am wondering whether many of the other patients have shown the tendency toward the production of similar atrophy.

So far as the direct question which Major Glicklich raised, I do not believe that there have been many more cases of lichen planus at our clinic or in my own practice than before. I think that every one is conscious of the discussions which arose at the meetings during the depression of 1931 and 1932 and at the time of the last war as to whether or not there were more cases occurring in times of nervous tension and excitement, but I think that it was generally agreed that they were no more prevalent. I think that this group is an extremely interesting one. I hope that something to follow can be worked out.

DR GEORGE E MORRIS, Boston. All these people have in common the fact that they took quinacrine hydrochloride (atabrine). I think that some of our patients with lichen planus should be given quinacrine hydrochloride to see if they show any change.

DR C GUY LANE, Boston. I should like to ask Major Glicklich if any of these patients have been given a course of bismuth.

MAJOR EARL A GLICKLICH, MC AUS. Some of them have had bismuth but not in full courses, others have had small amounts. They have had the usual course that was expected. A great many of those who have returned to the United States start to improve just as soon as they pass the equator. I have not given any specific therapy such as bismuth or mercuric salicylarsonate, the lesions soon improve, leaving pigmentation. In regard to quinacrine hydrochloride, patients have been seen who have not received quinacrine hydrochloride. At first it was thought that quinacrine hydrochloride might be the whole cause, but, as I stated, patients have been seen that have not received quinacrine hydrochloride. A great many of them have had sulfonamide drugs but not all of them. As regards the beginning of some of these lesions, 2 of the boys and a great many other patients have given a story that they began to have vesicular lesions on the extremities, particularly the fingers and feet, a picture similar to a fungous infection, and then the lesions blossom into a lichen planus. Some of the patients have lost a great deal of weight. As far as atrophy is concerned, some infections go on to atrophy and some go on to hypertrophic lesions.

DR FRANCIS P MCCARTHY, Boston. I am interested to know whether the cases of lichen planus were confined to the New Guinea Area. This island is recognized as one having the most enervating climate in the South Pacific, and combat service over a long period is attended with physical exhaustion, mental depression and loss of weight.

MAJOR EARL A GLICKLICH, M C, A U S So far as I recall the cases of this group, I have seen only those that have come from New Guinea. I have not seen them come from other areas. What Dr McCarthy says is true, there is probably more depression in that area, but some of these eruptions developed immediately, those, for example, in these 3 boys, I do not believe that they were in that area more than eight months to a year. They have not lost too much weight, but others at the hospital have lost 40 to 60 pounds (18 to 27 Kg). I do not know whether the eruption is caused by the diet or whether it is on a basis of nerves. I am inclined to sway to Dr Lane's way of thinking that this dermatosis is of a bacterial or a virus nature which as yet cannot be determined.

DR C GUY LANE, Boston Do you know what the earliest incubation period is?

MAJOR EARL A GLICKLICH, M C, A U S I cannot answer that definitely, but I think that it is within a period of six months.

DR VINCENT J RIAN, Providence, R I Would you say that the vast majority of cases occur in New Guinea?

MAJOR EARL A GLICKLICH, M C, A U S Yes, I should.

#### Lupus Erythematosus and Dermatitis Venenata Presented by DR C GUY LANE, Boston

A B, a 36 year old man, an Italian welder, presented lesions on the face, of two years' duration, and an acute eruption, of three weeks' duration, involving the chest, back, axillas, genitalia and perineum. Photophobia was intense. He had been receiving gold sodium thiosulfate intravenously for the past two years. Two weeks after the onset of the acute weeping exacerbation, the administration of gold sodium thiosulfate was discontinued.

Examination reveals maculopapular, brilliant red and oozing lesions involving the eyelids, chest, upper portion of the back, axillas and scrotal and perineal areas.

Results of laboratory studies comprising blood count, urinalysis, nonprotein nitrogen tests and serum protein tests were within normal limits.

Colloid baths, moist boric acid compresses, antipruritic lotions and an antiseptic powder have produced little relief.

#### DISCUSSION

DR FRANCIS M THURMON, Boston The atrophic changes, grayish scaling, erythema and butterfly-shaped eruption across the bridge of the nose and malar areas leave no doubt as to the diagnosis of lupus erythematosus. However, when the young man was questioned, he stated that the eruption, which developed elsewhere, started in the scrotal-groin-thigh areas and the axillas. The character of this dermatitis, which is red, macular, papular and moist, suggests a dermatitis venenata due to resin-finished facing in cotton underwear. As is known, the cause of this dermatitis was found to be an ester gum made from abietic acid and a special type of alcohol used in the facing of underwear, shirts and pajamas. This patient has a mixed type of eruption. I doubt that the red, round and oval macular and papular lesions on the extremities are a dermatitis medicamentosa precipitated by gold sodium thiosulfate.

DR GEORGE E MORRIS, Boston This man is a welder. It is well known that welders are exposed to ultraviolet light (this man stated that he has had two flash burns), I wonder about the advisability of permitting a man with lupus erythematosus to work as a welder. We have had 1 case, that of a Negro girl who died of lupus erythematosus and who had no trouble until she began welding. How do the members of the society feel about this problem?

DR FRANCIS P MCCARTHY, Boston Exposure to ultraviolet radiation is generally accepted as being an activating factor in lupus erythematosus.

DR C GUY LANE, Boston When I suggested that this patient be shown, I intended to present the case for diagnosis rather than to have a definite

diagnostic statement    He was to be shown as a patient with lupus erythematosus, with the question as to whether there was a superimposed contact dermatitis, seborrheic dermatitis or a dermatitis medicamentosa    I might say that the picture has changed a good deal since his present entry to the hospital    The treatment was followed by Dr Maurice M Tolman and more recently by Dr Carl S Sawyer    The patient had gold sodium thiosulfate, and, as I gathered from the history, an eruption developed on the scrotal area first, then, I think, he had two or three more additional treatments with gold after the original eruption developed and an increasing extension of the eruption and new areas, so that the gold was stopped    He had a phenol lotion, but I do not know whether or not he had something with salicylic acid    Then he had a moderate amount of scalp involvement    There was a question as to the etiologic factor    When he entered the ward, he was a "mess," with acute oozing red areas on the face, so that these areas of lupus erythematosus were well blocked out    There was a great deal of redness in the axillas and in the groins    That has subsided under boric compresses and relatively soothing treatment    I could not help feeling that the gold did not do him any good    I think that it tipped the scales unfavorably after the original exacerbation    I did not know until Dr Morris mentioned it that he was a welder    My reaction to that would be that I know all the welders I know are shielded pretty well with their hoods    Probably occasionally they slip up    I think that their goggles are impervious to ultraviolet rays    I think that in the presence of lupus erythematosus he should not be exposed to ultraviolet rays and that he should have a different job

**Acne Vulgaris**    Presented by DR GEORGE E MORRIS, Boston

R G, a white male infant aged 9 months, presented an acneform eruption, of five months' duration    Examination revealed comedos, pustules and papules on the forehead and cheeks    Examination of the blood showed a hemoglobin content of 80 per cent and a leukocyte count of 7,500, with a differential count of polymorphonuclear leukocytes 75 per cent, lymphocytes 20 per cent, mononuclears 4 per cent and eosinophils 1 per cent    The urine was normal    Roentgenologic examination of the bones showed development consistent with that of a 2 year old child

DISCUSSION

DR LEONARD E ANDERSON, Springfield, Mass    I have seen frank comedos in perhaps 2 or 3 infants of this age and younger    They have never been so pronounced as this or well enough developed to be dignified with the name "acne vulgaris"    With mild treatment, they improved

DR C GUY LANE, Boston    I have seen 1 other case, that of a child of 18 months, in which there were pronounced acne lesions    I have also seen 2 other cases of precocious development of acne in patients at a later age, about 10 or 12 years, the acne in both cases was extremely active    One of the patients later turned out to have a hypernephroma and the other turned out to have something which I suspect was hypernephroma, because operation on his kidney was performed, with a fatal outcome    I do not know that all children with a precocious development of acne have that happen to them but at least there are 2 cases of precocious development of severe acne in which that happened

DR WALTER F LEVER, Boston    I should like to ask if this child was treated with salves, first with one containing sulfur and then with one containing ammoniated mercury?

DR JACOB H SWARTZ, Boston    I suggest a diagnosis of *nevus comedonicus*    It is not a typical case    In the few cases I have seen the eruption has been localized and has shown more miliary-like lesions with comedos    Of course, a dermatitis is superimposed because the child has a dermatitis on his arms    I suggest a biopsy to see whether a diagnosis of *nevus comedonicus* rather than *acne vulgaris* could be established

DR LEONARD E. ANDERSON, Springfield, Mass. Does not nevus comedonicus occur as circumscribed areas but not as diffuse involvement?

DR GEORGE E. MORRIS, Boston. It is important to ask the mother the occupation of the father, for rashes similar to this have been seen in babies whose fathers have worked either with one of the chlorinated naphthalenes or with the diphenyls, which are used as insulating materials, especially on ships. In children comedos of the face develop if the father works with such materials and fails to change his clothing before coming home and holding the baby. Interestingly, the father works in the navy yard as an electrician but is an instructor and does not come in contact with any of the insulation materials. Roentgenograms show that the child has an abnormal bone age, which suggests an underlying endocrine cause for his trouble. To Dr Lane's case I can add a third, that of a girl who had preadolescent acne and who finally was proved by operation to have bilateral adrenal cortical tumor. In her case, the diagnosis was not made until the age of 12, at which time all the epiphyses were united. The other endocrine gland which may be involved is the pituitary. More study on this case is necessary before the underlying cause of her eruption can be decided.

**Neurotic Excoriations, Raynaud's Disease** Presented by DR FRANCIS M. THURMON, Boston

N. N., a white American housewife aged 46, presented lesions on the neck, chest and shoulder, which had been present intermittently during the past fifteen years. Following scarlet fever, itching lesions began to develop on the areas previously noted. The patient would "dig out" these lesions, thus relieving the itching, crawling sensation. Also, her fingers and toes have been blanching white and aching on exposure to cold for several years.

Examination reveals depressed small scars and a few freshly excoriated papules on the neck, chest and shoulder. Laboratory examination, including the Hinton, Wassermann (Kolmer) and Kahn tests of the blood revealed nothing abnormal, and examination of the urine, blood sedimentation rate and blood count gave normal results.

DISCUSSION

DR JACOB H. SWARTZ, Boston. I remember that, as a student, Dr Charles J. White used to label such cases "Pick's disease." More excoriations were seen on the upper portion of the back than on the chest. A better name is "neurotic excoriations." That explains the disease better than "factitia" when dermatitis factitia is considered as an external form of laceration. This patient has a history typical of Raynaud's disease, wherein her hands turned snow white on exposure to cold, with cramps. I think that it should be labeled Raynaud's disease with neurotic excoriations.

DR FRANCIS P. MCCARTHY, Boston. Is there not a history of acarophobia in this case? The acarophobic patient deliberately picks at small particles of epithelial debris or dirt, believing that they are parasites, and excoriates himself as a result of self-inflicted trauma.

DR C. GUY LANE, Boston. Does anybody know what has happened to the term "dermatoplasia" which was given to this condition at one time?

DR FRANCIS M. THURMON, Boston. I was of the impression, since she so cheerfully admitted the fact, that she was conscious of what she was doing. She is fundamentally a nervous woman. She stated that there are itching sensations and sometimes there is a small papule or elevation or roughness of the skin, she is not happy until she digs that particular lesion, and then the itching disappears. The distribution is over the upper portion of the chest and shoulders. On the back, on areas she cannot reach, there are no lesions. We thought that this was an example of neurotic excoriations. There are occasional cases of dermatitis herpetiformis with sparse but symmetric distribution such as this patient presents in her scars. It can be localized to particular areas of the body, but the absence of typical

lesions of dermatitis herpetiformis led to the diagnosis of neurotic excoriations Raynaud's disease involving the fingers and toes is evident

**A Case for Diagnosis (Dermatitis Factitia? Gumma of the Right Great Toe and Chronic Osteomyelitis of the Right First Metatarsal and Left Tibia? Epithelial Sinus?)** Presented by DR BERNARD APPEL, Lynn, Mass, and DR GEORGE E MORRIS, Boston

J M, a white woman, a 47 year old clerk, presents lesions of the right great toe and left tibia, of approximately twenty-eight years' duration. The onset was marked by a blister on the right great toe, which became infected and apparently healed within three weeks. Frostbite in the toes the following winter was characterized by edema, purplish discoloration and desquamation. During the subsequent eight years, the right great toe appeared "inflamed," and a continuous burning sensation was noted. During the eighth year, the toe became ulcerated, it was treated, and it healed within six weeks. During the next five years, the ulceration recurred on three occasions and healed completely, on the fourth occasion it remained open. Also throughout this twenty-eight year period, an osteomyelitis of the left tibia has been present. Eight years ago an examination of the cerebrospinal fluid was made, and it was reported normal.

Examination reveals a red, granulating, nonpainful, sharply demarcated ulceration of the right great toe, which is surrounded by sclerodermatous scarring. A large draining sinus of the midportion of the left tibia is present.

The Hinton reaction of the blood was negative. The hemoglobin content was 12.5 Gm, and the leukocyte count 12,400, with a differential count of polymorphonuclears 65 per cent, lymphocytes 32 per cent, large mononuclears 1 per cent and eosinophils 2 per cent. At examination the urine was normal. The blood cholesterol determinations were 349 and 264 mg per hundred cubic centimeters. Fasting blood sugar was 87 mg per hundred cubic centimeters. The congo red test elicited a negative reaction. The basal metabolic rate determination was minus 11 per cent. *Staphylococcus aureus*, *Streptococcus hemolyticus*, *Bacillus pyocyaneus* and *Bacillus proteus* were obtained by cultures from each lesion. Roentgen ray examination of the toe showed irregular thickening of the cortex of the first metatarsal, suggesting syphilis, and a cystlike degeneration of the distal end of the great toe. An old destructive process involved the proximal phalanx of the second toe. A localized osteomyelitis and cortical thickening of the lower portion of the left tibia, suggesting syphilis, was present. A biopsy of the lesion of the right great toe showed acute and chronic inflammation with ulceration and no evidence of gumma.

Potassium iodide, 30 minims (1.85 cc) administered three times daily, produced no change. The lesion of the toe appears improved under the local application of tyrothricin.

#### DISCUSSION

DR ALSTIN W CHEEVER, Boston. I did not see any evidence of syphilis. I am not ready to offer a diagnosis. I do not know that all these things can be put together under one diagnosis.

DR FRANCIS P MCCARTHY, Boston. I do not remember seeing the histologic section, but I do know that with a lesion with a surface layer of granulomatous tissue it is desirable to get a representative piece of tissue for biopsy and to cut deep enough to include tissue underlying the inflammatory zone of granulation tissue. I do not know whether or not a representative biopsy was presented in this case.

DR WALTER T GARFIELD, Boston. I agree with Dr Cheever. I could not see anything of a syphilitic nature. It seemed to me that there was a possibility of a low grade infection, with granulomatous tissue forming. That is as far as I should go.

DR FRANCIS M THURMON, Boston. I saw evidence of syphilis in the roentgenograms of the bones of the toes. The right great toe showed periostitis. The

midphalanx of the left second toe showed areas of rarefaction and bone destruction. In other words, there is formation of bone and destruction of bone going on in a chronic lesion which certainly can be interpreted roentgenologically as due to syphilis. As judged from the clinical appearance of the lesion and its indolent granulomatous character, syphilis is indicated. I also believe that there is present an element of malignancy and that if response to fever therapy should be negligible, amputation should be considered.

DR FRANCIS P MCCARTHY, Boston. Did you have a chance to see the roentgenograms in this case? Were you able to make any interpretation?

DR AUSTIN W CHEEVER, Boston. My feeling was that syphilis was not present. I was not ready to make a diagnosis.

DR C GUY LANE, Boston. May I ask if the patient had any antisyphilitic treatment?

DR GEORGE E MORRIS, Boston. She had some bismuth and a few doses of oxophenarsine hydrochloride but not any intensive antisyphilitic therapy. I was uncertain as to whether it was syphilis.

DR FRANCIS M THURMON, Boston. In syphilis of the bone, serologic reactions of the blood for syphilis are notoriously negative, likewise, the results of mixed chemotherapy are often disappointing. It is amazing what fever therapy will do in a patient of this type. In a patient so hospitalized, at least fever therapy along the lines of foreign protein administered intravenously can be carried out.

DR WALTER F LEVER, Boston. I want to suggest that a larger specimen be taken for histologic examination. The slide showed only granulation tissue, but I am sure that something more will be found if a deeper incision is done.

DR ALFRED HOLLANDER, Springfield, Mass. I believe that the lesions are caused by artefacts. Two new lesions are seen in this case, and I believe that these lesions are a result of picking or scratching. Such cases are seen frequently. There are many persons whose skins respond to intense scratching with scaling and pigmentation. Cases of such eruptions are described in the literature, and I think that a few of them are illustrated in the "Corpus Iconum Morborum Cutaneorum" (Leipzig, Johann Ambrosius Barth, 1938) and are called "pathomimia."

#### **Keratitis, Syphilitic, Congenital** Presented by DR LEO KORETSKY, Chelsea, Mass

M. D., an Irish housewife aged 45, presented an inflammation of the right eye, which was of four weeks' duration. The onset was marked by redness, increased lacrimation, pain, photophobia and blurring of vision. There was no history of early syphilis. The family history was inadequate, one brother was living and well in Ireland, and her father and mother were deceased there.

Examination reveals an injection of the conjunctiva and sclera of the right eye. Her hearing is normal. Six lower front teeth are present, the remainder had been extracted at an early age.

The Hinton, Wassermann (Kolmer) and Kahn reactions of the blood were repeatedly positive. The urine was normal.

Improvement was noted following two treatments with bismuth subsalicylate.

#### DISCUSSION

DR AUSTIN W CHEEVER, Boston. I found no proof of congenital syphilis. There were six blood tests reported positive for syphilis, which seems to show that she has syphilis, and the age of 45 is not out of bounds for the interstitial keratitis to appear. I had 1 patient, aged close to 40, with a similar disease in the old South Department for Infectious Diseases of the Boston City Hospital. Dr Stokes has reported 2 or 3 cases of interstitial keratitis occurring late in life. I am willing to accept that diagnosis.

DR G MARSHALL CRAWFORD, Brookline, Mass Has there been a slit lamp examination?

DR FRANCIS M THURMON, Boston Not yet

DR G MARSHALL CRAWFORD, Brookline, Mass I think that there have been cases reported in which ariboflavinosis and vitamin E deficiency were found in which the ocular changes were indistinguishable from the interstitial keratitis of congenital syphilis but they could be differentiated by slit lamp examination That should be done, although the patient shows no other evidence of syphilis

DR FRANCIS M THURMON, Boston This patient was seen in consultation by Dr Joseph J Skirball, chief of the eye clinic at the Boston Dispensary He made a diagnosis of interstitial keratitis The thought that a riboflavin deficiency could produce an interstitial keratitis is intriguing Repeated serologic reactions of the blood have been positive for syphilis The patient has received only a few injections of bismuth, and with those injections there has been a definite improvement in the interstitial keratitis I believe that this is congenital syphilis, since with that entity the greatest frequency of interstitial keratitis is seen I thought that this case was particularly interesting because of the onset of the disease in a patient at the age of 45

#### A Case for Diagnosis (Syphilitic Ulcer?) Presented by DR GEORGE SCHWARTZ, Malden, Mass

M H, a Negro man aged 66, presented an ulceration, of ten years' duration, involving the left leg and discrete round and oval crusted lesions, of two years' duration, involving the groins, abdomen and chest At the onset the ulcer of the leg was small, and it healed under conservative treatment However, it recurred in 1943 and has grown progressively larger

Examination reveals a large ulceration over the anterior surface of the left leg It is comprised of clean granulation tissue with well defined circinate margins which are surrounded by deep cicatrices The lesions of the groin, abdomen and anterior portion of the chest are discrete, circinate and crusted

Examination of the blood shows a hemoglobin content of 9.5 Gm and a leukocyte count of 5,900 The results of the examination of the urine were normal Nonprotein nitrogen was 27 mg per hundred cubic centimeters A roentgenologic examination of the long bones of the left leg showed periostitis

#### DISCUSSION

DR AUSTIN W CHLEVER, Boston I do not agree with the diagnosis of syphilis in this case There is decided symmetric distribution of the lesions under the breasts and down the flanks, but to my mind that is entirely different from the type of border in tertiary syphilis It is not ulcerated as far as I can see, and there are even sweeping curves I think that the ulcer could possibly be of a syphilitic nature, but I rather doubt it I am inclined to suggest a vitamin deficiency, a pellagra of an unusual sort I have seen 1 case of pellagra with the general type of lesion that this patient shows, a case of eruption around the breasts in a woman who ate practically nothing but spaghetti and tomatoes and who improved on a normal diet fortified with vitamin B

DR ADRIAN H SCOTTEN, Portland, Maine I asked her about her diet She said that she ate no lamb, beef, pork or chicken When I asked her what meat she did eat, she answered, "Occasionally a little hog meat" I discovered that she did not like milk Based on an experience of six months in a hospital for Negro patients down South, I should say that the disease in this patient resembles malnutrition which Dr Joseph Grindon Sr would call pellagra

DR GEORGE SCHWARTZ, Malden, Mass I understand that the roentgenograms show a periostitis of both tibiae

**A Case for Diagnosis (Neurofibromatosis with Sarcomatous Changes?)**

Presented by DR GEORGE SCHWARTZ, Malden, Mass

P P, a white schoolboy aged 17, presented cutaneous tumor masses of generalized distribution. Since childhood, several soft tumor-like masses have been present on the left shoulder, back and right leg.

Lentigenes are generalized. Of the profuse and generally distributed pigmented macules which vary in size and shape, some are coffee colored and others are a dark brown. Soft, oval, sessile masses are variously distributed over the cutaneous surface. Numerous, deep, firm, subcutaneous masses are present, involving especially the right arm and neck.

Laboratory studies, including blood counts, agglutinations and urinalysis, were normal. The Hinton reaction of the blood was negative.

## DISCUSSION

DR ALFRED HOLLANDER, Springfield, Mass. I do not believe that true von Recklinghausen's neurofibromatosis can change into a malignant growth.

DR WALTER F LEVER, Boston. I want to take exception to that statement. I have encountered 2 cases of von Recklinghausen's neurofibromatosis in which sarcomatous lesions developed. One I saw recently. In this case a lesion of the thigh was first examined histologically eight months ago and showed von Recklinghausen's neurofibromatosis. Ten months later the lesion began to grow rapidly and again was examined histologically. It showed sarcomatous changes (Case 30401, *New England J Med* **231** 496 [Oct 5] 1944).

DR GEORGE SCHWARTZ, Malden, Mass. The patient has a similar lesion on his hand. A biopsy was taken, but the report has not been returned.

**Dermatitis Exfoliativa** Presented by DR EDWARD A LAFRENIERE, Arlington, Mass

S B, a Jewish man aged 54, a florist, presented a generalized eruption, of ten months' duration. The onset was marked by lacerations of the hands by rose thorns, which became secondarily infected and were bathed with saponated solution of cresol. Erythema and pruritus resulted, which shortly thereafter became generalized.

Examination reveals generalized erythema, edema and scaling. The hands and feet are fissured. The nails are dystrophic and opaque. There has been complete loss of nails on three occasions since the patient's admission to the hospital. Pruritus is intense.

Results of a blood examination showed a hemoglobin content of 83 per cent and a leukocyte count of 10,300 with a differential count showing polymorphonuclears 76 per cent, lymphocytes 13 per cent, mononuclear leukocytes 1 per cent and eosinophils 10 per cent. The nonprotein nitrogen of the blood was 30 mg per hundred cubic centimeters. The Hinton reaction of the blood was negative, and a urinalysis was normal.

There was no response to colloid baths, lotions or ointments topically applied or the intravenous administration of calcium gluconate. Moderate improvement was noted after roentgen therapy to the back and ankles.

## DISCUSSION

DR FRANCIS P MCCARTHY, Boston. This is probably the most interesting case shown today. It brings up the question of whether a dermatitis that starts as contact dermatitis or dermatitis venenata and gradually spreads either by sensitization or by other means can become dermatitis exfoliativa. It is generally appreciated that the vast majority of cases of dermatitis venenata are caused by endogenous conditions, such as those due to the arsenicals or various drugs. However, there are occasional occupational dermatoses that begin as local processes that may end as generalized dermatitis exfoliativa.



DR C GUY LANE, Boston In our ward a number of cases are seen in which the original lesion is a localized lesion which may be the result of trauma or a low grade infection or simply an irritation which, as time goes on, under the impetus of therapy becomes wider and eventually becomes more generalized I think that those are seen more frequently in the winter than at any other time I have no hesitation in saying that exfoliative dermatitis can arise from contact, from therapy or from one's occupation I do not believe that it needs to have an endogenous origin As far as the occupational factor goes in this state, not only the occupational disease as such is subject to compensation, but the complications of the occupational disease may be compensatory as well as the cutaneous disease exaggerated by the occupation Both may come under the law in the states in which the schedules apply and the disease is listed I do not think that applies in all states, I do not know how many states there are whose interpretation is as broad as it is here

DR FRANCIS M THURMON, Boston The cutaneous response, especially on the hands, fingers and palms, certainly was a keratoderma not unlike some rare cases of keratosis blennorrhagica which are seen Penicillin is a specific therapy against gonococci, and I wonder what the response of this patient would be to penicillin therapy I think that it might be worth trying

DR C GUY LANE, Boston In these cases, I am much interested in what the first therapy has been I do not care whether the eruption begins on the ankle or on the hand I think that the early therapy, particularly in these days of sulfonamide sensitization, often could explain a good deal if it could be known The sensitization by the early therapy often plays a part in the general sensitization that results in dermatitis exfoliativa in the end

DR EDWARD A LAFRENIERE, Arlington, Mass I have not seen the patient for three months, and he has improved The eruption will probably flare up again in the next three months

#### **A Case for Diagnosis (Moniliasis of Groins and Submammary Folds?)**

Presented by DR GEORGE E MORRIS, Boston

E M, a white American housewife aged 50, presented lesions, of four weeks' duration, which primarily involved the genitocrural folds and breasts The present illness began with pruritus vulvae Soon thereafter lesions appeared on the genitocrural folds, trunk and extremities

Examination reveals a suffused, moist, erythematous eruption and partial desquamation of the skin on the perineum, medial portion of the thighs, pubis and submammary folds Macular, papular and dusky red, crusted lesions varying from 0.5 to 1.5 cm in diameter, some of which show scaling, are scattered over the arms and back

Aside from a normal urinalysis, other laboratory studies have not been reported

#### **DISCUSSION**

DR MILDRED RYAN, Brockton, Mass I thought that she had a seborrheic type of psoriasis Her scalp is covered with thick scales She has plaques on the elbow

DR ALFRED HOLLANDER, Springfield, Mass I think that the obesity and the resulting perspiration, together with a possibility of diabetes, are the etiologic factors in this case

DR JACOB H SWARTZ, Boston I think that the diagnosis of moniliasis should be made with much caution The diagnosis should be checked by culture, and *Monilia albicans* must be grown, since other nonpathogenic yeasts may be present but play no etiologic role I did not see the lesions of the elbows and the scalp, but I got the impression that this woman has intertrigo with secondary bacterial infection, perhaps on a diabetic basis

**Dermatitis Medicamentosa (Due to Sulfadiazine)** Presented by DR GEORGE E MORRIS, Boston

C P, a white Italian housewife aged 55, presented an eruption, of six days' duration, involving the neck and all extremities. The lesions appeared after the administration of sulfadiazine lozenges and a medicine containing codeine, acetylsalicylic acid and acetophenetidin, which were prescribed for a sore throat.

Examination reveals erythematous, painful, subcutaneous nodules involving chiefly the extensor surfaces of the legs. Small, oval, erythematous macules are seen on the anterior surface of the neck. Red, slightly elevated plaques, 5 by 7 cm, are symmetrically distributed on the arms. The joints of the fingers are swollen, and purple discoloration is present on the knuckles.

Examination of the blood revealed a hemoglobin content of 10 Gm and a leukocyte count of 7,300, with a differential count of polymorphonuclears 76 per cent, lymphocytes 23 per cent and mononuclear leukocytes 1 per cent. The blood sedimentation rate in twenty minutes was 1 mm and in one hour 7.5 mm. Examination of the urine showed  $pH$  6.5 and specific gravity 1.029. There was no albumin and no sugar, but bile was present (1 plus). The urinary sediment contained 8 to 10 leukocytes per high power field and a few granular casts.

DISCUSSION

DR JACOB H SWARTZ, Boston. She had sulfonamide pills, and I understand that codeine, acetylsalicylic acid and acetophenetidin were used just prior to the eruption, whereas the sulfonamide drug was stopped four days before the eruption appeared.

DR GEORGE SCHWARTZ. On December 4, she had grip. At that time she was given two powders containing codeine, acetylsalicylic acid and acetophenetidin. On December 7 she had a sore throat and was given sulfadiazine lozenges. She was seen again on December 9. She had a lesion on the forearms five days after she was first seen. On December 7, no lesions were seen on the forearm. The patient took only 3 lozenges of sulfadiazine at that time.

DR LEON BABALIAN, Portland, Maine. It is neither an allergic reaction nor a toxic reaction. I have a feeling that it is a biotrophic reaction of Milian, the infective agent of erythema nodosum having been reactivated by a drug.

DR MILDRED RYAN, Brockton, Mass. There was a case at the Massachusetts General Hospital similar to this one, in which purpuric lesions not unlike those of this patient developed as a result of the use of sulfonamide drugs.

DR JACOB H SWARTZ, Boston. I am going to raise issue on the question of activating the relative sensitivity to a drug. An erythema-nodosum-like eruption can be obtained by the administration of ethyl iodide. The patient did not have any bacterial infection prior to the administration. She had a fungus infection, and no fungus produces such lesions and yet I saw erythema-nodosum-like lesions following the administration of iodide. I naturally assumed that it was the iodide, and not the activation of the organism. I should favor the diagnosis of activation of it by the drug.

DR ALFRED HOLLANDER, Springfield, Mass. Some of the lesions, especially on the patellar region, appeared to me to be lesions of a fixed drug eruption. Those lesions should be separated from the erythema nodosum lesions in the middle third of the leg, especially the one on the patella.

DR GEORGE E MORRIS, Boston. If those are erythema-nodosum-like lesions, they are probably not due to sulfadiazine. As far as I know, the only sulfonamide drug which causes such lesions is sulfathiazole. Therefore the talk should be about codeine, acetylsalicylic acid and acetophenetidin unless some one has seen these lesions caused by another drug of the sulfonamide group.

DR G MARSHALL CRAWFORD, Brookline, Mass. There is a first time for everything.

**Dermatitis Medicamentosa (Due to Arsenic)** Presented by DR EDWARD A LAFRENIERE, Arlington, Mass

F T, a white American woman aged 33, presented a generalized dermatitis of two weeks' duration. The patient had been treated by her local physician with intravenous injections for syphilis at seven day intervals over a period of a month. The second treatment was followed by nausea, vomiting, fever and chills. After the third treatment a transient generalized eruption resembling measles appeared, which lasted only four days. The fourth treatment was followed by nausea, vomiting, chills and fever, the morbilliform rash recurred. Seven days later an intramuscular treatment was administered. The eruption, which was still present, became accentuated and was characterized by heat, edema, dryness and desquamation especially on the palms and soles.

The entire body surface is glistening red, warm, dry and scaling. The palmar and plantar skin has desquamated in large plaques, leaving raw, red, denuded surfaces.

The Hinton reaction of the blood was positive. Examination of the blood showed a hemoglobin content of 10 Gm and a leukocyte count of 11,850, the differential count showed polymorphonuclears 54 per cent, lymphocytes 25 per cent and eosinophils 21 per cent.

Treatment has comprised starch baths, calamine lotion and moist boric acid dressings to the face and hands. Caffeine, hot drinks and high vitamin diet have been administered.

## DISCUSSION

DR C GUY LANE, Boston: One thing that interested me in the history was the fact that after two injections following the beginning of the eruption it quieted down and then the intramuscular injection, which I suppose was bismuth, was given. Is that true?

DR JACOB H SWARTZ, Boston: There was an intramuscular injection.

DR C GUY LANE, Boston: This is a case of an activation by another drug that sounds like bismuth. I think that happens in cases of this type and occasionally bismuth is a contributing factor in the cases of jaundice as well.

DR FRANCIS P MCCARTHY, Boston: It might be said that it is the rule rather than the exception in my experience with the cases of fatal arsenical poisoning for the practitioner to use the maximum dose rather than the small dose which is administered by hospital clinics. Usually in the hospital group neoarsphenamine is administered in 0.3 Gm and occasionally in 0.45 Gm amounts, whereas in general practice 0.9 Gm is frequently used as a routine since it is considered the proper maximum dosage and is so listed on the package.

## CHICAGO DERMATOLOGICAL SOCIETY

Lester M. Wieder, M.D., *President*

Marcus R. Caro, M.D., *Secretary*

Dec 20, 1944

**Idiopathic Macular Atrophy** Presented (by invitation) by DR S ROTHMAN and DR HELFN KRISA

B. B., a 50 year old housewife, born in Lithuania, was admitted to the neurology service of Albert Merritt Billings Hospital on Dec. 10, 1944 for the investigation of a sciatic type of pain on the left side of one year's duration.

Twelve years ago the patient noticed a discoloration in the sternal region. This change of color was not preceded by trauma or by any inflammatory sign or symptom. Gradually this "soft" lesion increased in size and became redder. Light

years ago a similar lesion developed on the left upper part of the back. Two years ago two more lesions made their appearance on the lower left side of the chest, and one year ago three or four lesions appeared on the right shoulder.

All the lesions are sharply circumscribed. They display loose atrophy with cigarette paper folding, and on palpation a defect can be felt. Some of them are surrounded with a faint reddish blue hue. The smaller lesions, particularly those on the sides of the chest, show considerable herniation. Most lesions are depigmented, but tiny hyperpigmented spots also are seen within the large lesion of the sternum.

The sections stained for elastic fibers showed atrophic epidermis, lack of appendages and almost complete absence of elastic fibers (Virchow's stain).

The Wassermann and Kahn reactions of the blood were negative. The blood and differential counts and the urine were normal. The basal metabolic rate was —8 per cent. The roentgenogram of the chest showed slight enlargement of the left ventricle. The electrocardiogram was within normal limits. The myelogram showed a filling defect in the segments of the first and second lumbar vertebrae, suggesting an intramedullary tumor, and also a filling defect in the fourth and fifth lumbar vertebrae, suggesting a ruptured disk.

#### DISCUSSION

DR M. H. EBERT: For many years I have been interested in seeing a unique case of anetoderma as described by Jadassohn. In his original article the final result was exactly what is seen today in this patient. At some time early in the history of the lesion it was inflammatory and infiltrated. Dr. Rothman stated that some of the lesions have had an areola of slight erythema but no definite infiltration. Perhaps he will tell us whether the eruption is an anetoderma of Jadassohn.

DR MAURICE OPPENHEIM (by invitation): About three months ago I presented to this society a classic case of anetoderma erythematosa of Jadassohn. All the three stages of the disease, which I described in my article on this disease in the *Archiv für Dermatologie und Syphilis* about forty years ago, were present: the stage of erythema circumscriptum, the stage of forming rings with a wrinkled center, and the last stage, the formation of hernia-like protuberances, which, like a hernia, are removable by digital pressure.

I think that the case presented by Dr. Rothman is one of macular dermatitis atrophicans, starting twelve years ago, but there is present only the last stage of this disease. The hemorrhagic changes remind me of the case which Drs. Schweninger and Buzzi described as one of a macular cutaneous atrophy. In my papers about the diffuse and macular cutaneous atrophy I stressed the opinion that the case of Drs. Schweninger and Buzzi was one of von Recklinghausen's disease with resorption of the tumors in certain areas.

DR HAMILTON MONTGOMERY, Rochester, Minn.: I think that this disease could be called an anetoderma of Jadassohn. One must keep in mind the fact that macular atrophies arise secondary to syphilis, leprosy and many other dermatoses. Multiple benign tumor-like new growths of Schweninger and Buzzi are not related to von Recklinghausen's disease (neurofibromatosis). Macular atrophic lesions in von Recklinghausen's disease histologically still reveal evidence of neurofibromatosis and do not show the histologic changes of the group of macular atrophies.

DR FRANCIS E. SFNEAR: This society had an experience that illustrated the confusion that may exist in such a situation. Many years ago Dr. Pusey described the first case of tumor-like new growths recorded in this country. That was a typical example of that disorder. Some years later there was presented from the University of Illinois a Negro girl who had lesions that were clinically exactly the same in appearance as those in the case described by Dr. Pusey. I also saw the first patient. She had many herniated lesions underneath the scapula, which were clinically of the Schweninger-Buzzi type. In the case of the girl who was presented some years later, everybody who discussed it agreed that it was a typical case of benign tumor-like new growths. About five years later Dr. Oliver showed

a presumably new patient with a typical Recklinghausen's disease. She had cafe-au-lait spots. It was eventually found that she was the same patient presented several years previously in an early stage, with the diagnosis of Schweninger-Buzzi disease, but at the second presentation the picture was typical of neurofibromatosis.

DR H. E. MICHELSON, Minneapolis. I had the privilege of seeing Dr. Pusey's patient, and I also had the patient on whom Dr. Sweitzer reported. I do not believe that the Schweninger-Buzzi condition should be called a disease. It is merely an observation, and for my own part I think that it belongs to the macular atrophies.

DR S. ROTHMAN (by invitation). I feel sure that Jadassohn would have called this eruption anetoderma, because I saw a patient with a disease identical with this one that he diagnosed as such. On the other hand, I think that the initial erythema in this disease has been overemphasized in the literature. There is a slight initial erythema, but it appears rather early, as Dr. Oppenheim said, and disappears soon. It is rather depressing that so little is known about the pathomechanism and cause of idiopathic atrophies.

**Raynaud's Disease** Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS

F. S., an Italian-American shoemaker aged 58, presents an eruption of three years' duration involving the distal areas of the extremities. The fingers and toes are of a dusky reddish color and are cold to the touch. There are pinhead-sized necrotic spots which occur at irregular intervals, especially during the cold season of the year, although the patient is never free from pain, even in the summer.

In November 1941 the right great toe was involved in a similar process which resulted in sloughing of the terminal segment of the bone, after which healing took place.

The patient was hospitalized at Cook County Hospital, and the results of all examinations were essentially within normal limits.

DISCUSSION

DR. RUBEN NOMIAND, Iowa City. Raynaud's disease occurs almost always in women and is practically unknown in men. This man had a much diminished pulsation in one of the arteries at the wrist, and I could not feel the pulse in his dorsalis pedis artery. I think that he has arterial occlusive disease, probably Buerger's disease, with vasospastic symptoms and changes from arterial occlusion.

DR. S. ROTHMAN (by invitation). I want to call attention to the confusion that exists in the minds of nondermatologic physicians particularly in the differentiation of Raynaud's disease and scleroderma with Raynaud-like signs ("acro-sclerosis"). The latter is a generalized disease of the connective tissue and as such also involves the connective tissue of blood vessels, whereas Raynaud's disease is a purely arterial disease. Raynaud's disease leads to the formation of gangrene within one year after the onset, whereas acrosclerosis does not. Sympathectomy had deleterious effects in cases of acrosclerosis.

**Sycosis (Generalized)** Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS

S. L., an Italian-American man aged 21, presents a pustular infection involving the face, axillas and anogenital area which has been present for seven years.

The case is presented because of the widespread involvement and to stimulate discussion on therapeutic possibilities.

DISCUSSION

DR. FRANCIS E. SENEAR. There was an article on penicillin in the *British Medical Journal*, which was abstracted in one of the columns of a local paper. On reading the summary, one found that sycosis barbae was about the only thing that

responded to penicillin I have not had experience with this drug, but perhaps it would be worth trying

DR JAMES H MITCHELL I tried penicillin locally in a mixture of Aquaphor (an oxycholesterol-petrolatum ointment base) and had excellent results I used it in the office a few times There was a patient here in the clinic, who responded to penicillin after having resisted everything I think that the use of penicillin is worth a trial

DR MAURICE OPPENHEIM (by invitation) I treated this patient for two years with roentgen rays applied to his face He is much improved today At the same time he had a severe seborrheic dermatitis on the scalp, eyebrows and pubic area I do not think that dermatologists have the right to call such cases ones of sycosis generalisata, since this name is limited to the beard What one has in this case is a superinfected seborrheic dermatitis, probably with staphylococci

DR HERBERT RATTNER At the local Army hospital, I saw a patient with severe sycosis barbae treated with injections and local applications of penicillin, with excellent results, but Major Saffron informs me that the treatment does not give good results in all cases

DR M H EBERT I am inclined to agree with Dr Oppenheim that the primary disease in this case is seborrheic dermatitis or eczema and that the infection is secondary I suggest the use of 40 per cent sulfur paste

DR DAVID V OMENS I am grateful for the amount of discussion on this case I have treated several patients having coccogenous sycosis with penicillin, and I have not had good results in these cases or in cases of acrodermatitis chronica continua (Hallopeau) I am sure, however, that sulfur paste offers possibilities which warrant a trial

MAJOR M H SAFFRON, M C, A U S At the recent convention of the Southern Medical Association Dr Morginson reported on 7 cases of sycosis vulgaris treated by penicillin intramuscularly and also by the local use of penicillin In all 7 cases there were complete failures in response to penicillin therapy I, myself, have had occasion recently to administer penicillin in 4 cases of generalized sycosis vulgaris of the same type as presented here today In no instance did I secure an entirely satisfactory result, even though doses as high as 1,000,000 units of penicillin were given In 1 case in which the organism was reported as being highly sensitive to penicillin the disease had previously resisted a course of penicillin administered intramuscularly My course, the second one, was likewise ineffective I personally am not convinced that penicillin is of great value in the treatment of chronic sycosis vulgaris

**Excessive Oiliness of the Skin and Paralysis Agitans** Presented by  
DR THEODORE CORNBLEET and (by invitation) DR DAVID COHEN and  
DR H C SCHORR

In a 51 year old white man there developed an excessive oiliness of the scalp and face four years ago and ten years after the onset of his symptoms of parkinsonism The patient is presented for his interest to dermatologists, to illustrate the known relationship between nerves and skin in this syndrome

#### DISCUSSION

DR HERBERT RATTNER Some years ago a group of cases of Parkinson's disease was reported, in which there was a peculiar hyperpigmentation on the face In every one of the patients the striking feature was the extreme oiliness of the face At that time I examined a group of some 35 patients, and every one of them exhibited a very oily skin

DR S ROTHMAN (by invitation) To explain the phenomenon of the "ointment face," the theory was advanced that there is an inhibitory center of sebaceous secretion in the midbrain and that if this center is destroyed by encephalitis a free

flow of sebum sets in. This theory was supported by experiments of Perutz, who destroyed the midbrains in rabbits and obtained great increase in the secretion of fat from the skin.

DR THEODORE CORNBLEET. Dr Rothman touched on the theory concerning the control of the secretion of oil. It is not known just exactly where that is. Various controls have been postulated for the control of the secretion of oil. Prominent among these is that which uses the endocrine glands. There is overlapping of both nerves and endocrine glands in many situations undoubtedly, as in diabetes insipidus. The part of the brain near or at the pituitary stalk is thought to be at fault, and this in turn influences the neighboring gland. In paralysis there is supposedly a release of extrapyramidal mechanisms which exaggerate the actions of parts concerned. The sebaceous glands fall into this group.

**A Case for Diagnosis (Lymphoblastoma?)** Presented by DR M. H. EBFRI and (by invitation) DR M. S. KAGEN

F. M., a white man aged 45, presents a generalized itching eruption. Aside from recurrent attacks of ringworm of the feet with a few transient vesicles on the fingers, he had no serious trouble until fifteen months ago. At that time, on the advice of a friend, he used packs of saponated solution of cresol on the feet. A weeping dermatitis appeared on the hands. After the use of sulfathiazole ointment the dermatitis soon became generalized. Since then he has been hospitalized four times in Los Angeles and has been in the Cook County Hospital, Chicago, for six weeks. Every time he returned to his home, apparently completely well, the eruption would break out again overnight. The present attack, of eight months' duration, has been continuous with exacerbations. In the Los Angeles General Hospital he had many scratch and patch tests. All the tests elicited negative reactions with the exception of the one with soap. In August, in Los Angeles, a biopsy was made of the skin and lymph node, but the pathologist reported no specific conditions. He has had a moderate amount of roentgen ray therapy and considerable ultraviolet ray therapy. His itching is severest when he is warm in bed at night. He gives no history of atopy. One intravenous injection of typhoid vaccine raised his temperature to 101 F but brought no significant improvement. His condition today is considerably improved over what it was on his admission to the hospital. At present he has a generalized papular eruption with moderate infiltration. The papules tend to be grouped, especially on the upper part of the back and shoulders, where the groups are oval with the long axis along the bend of cleavage. On the backs of the hands the lesions are lichenoid. Many of the lesions have a brownish tint. There is a well generalized lymphadenopathy.

A hematologic examination made on Nov. 30, 1944 showed hemoglobin, 87 per cent, neutrophils, 48 per cent, eosinophils, 21 per cent, lymphocytes, 21 per cent, and monocytes, 9 per cent.

On December 12 smears were made from bone marrow obtained by sternal puncture. The hematologist's report is as follows:

"The marrow is moderately cellular. Megakaryocytes appear to be normal. The count of nucleated red blood cells to the white blood cell count is approximately 1:3 or 1:4. There are large numbers of eosinophils, which probably represent a secondary phenomenon to a possibly underlying lymphoblastoma, evidence for which is found in the increased number of lymphocytes, some of which are extremely premature."

The pathologist's comment was that the sections indicated primary lymphoblastoma with eosinophilic reaction.

A biopsy section of the skin is presented.

#### DISCUSSION

DR S. W. BECKER. I think that clinically this is a typical case of the Sulzberger-Garbe type of exudative neurodermatitis. The man is Jewish; he has been

working hard, and he had an eruption which cleared and then recurred That is a typical history

DR S ROTHMAN (by invitation) I have 2 cases on record of lesions simulating premycotic plaques of mycosis fungoides with generalized lymphadenitis and excessive eosinophilia in the blood and tissues Intense generalized hyperhidrosis accompanied the intolerable itching I wonder whether those cases as well as the one presented belong to the entity described by Sulzberger and Garbe There is no histologic or hematologic evidence of lymphoblastoma in these cases

DR FRANCIS E SENEAR I think that in this case there is a good deal of resemblance to the disorder described by Sulzberger It seems to me that the eruption is much more uniform in type than in the cases I have seen and in the ones demonstrated by Sulzberger at one of the meetings of the American Academy of Dermatology and Syphilology He pointed out that in that disease an involvement of the forehead and of the external genitalia is a constant feature, and the history indicated that these parts had been involved in this case

DR HERBERT RATTNER This case reminds me of a similar case diagnosed as one of Sulzberger-Garbe disease by several dermatologists in various parts of the country It subsequently was proved to be a case of dermatitis due to wallpaper The case would seem to raise the questions as to whether or not the Sulzberger-Garbe disease was an entity and whether psychogenic factors necessarily play a causative role

DR L F WEBER I should like to ask what there is in wallpaper that could cause such a syndrome

DR HERBERT RATTNER I do not know, but I understand that Dr Oppenheim eventually traced the trouble to wallpaper The story I received was that the wallpaper in the patient's bedroom was of an imported variety After it was removed from the wall, there was immediate improvement of the dermatitis I know only what I was told—I myself did not follow the case to the end

DR MAURICE OPPENHEIM (by invitation) The patient came to me in May with a diagnosis of leukemia The hematologic findings were not compatible with a diagnosis of leukemia Now he is all right after mild conservative treatment The skin was much overtreated I kept him in a hospital with absolute rest for three months He is now working, and the blood count is normal

DR M H EBERT This patient is shown through the courtesy of Dr Cornbleet, in whose service he is I became interested in him on making rounds because Dr Leaf and Dr Pearl, who studied in New York, were convinced when we first saw him that he had all the earmarks of a Sulzberger-Garbe dermatosis and the history would fit in with that diagnosis He has been in the Cook County Hospital six weeks, and since admission he has improved and today does not present the picture he did when we first saw him

Because of two nodules on the back of the hands and the nodular-like lesions on the other parts of the body, it was suggested that the eruption might be a lymphoblastoma, but the section did not bear this out A sternal puncture was made, and the observations suggested to the hematologist that it was an early lymphoblastoma That would account for the high eosinophil count It remains to be seen whether or not there will be a new flare-up

**A Case for Diagnosis (Lymphoblastoma?)** Presented by DR HERBERT RATTNER and (by invitation) DR H RODIN and DR M S KAGEN

A 57 year old white woman entered the Cook County Hospital with a history of cough for two years, loss of weight of 40 pounds (18 Kg), a daily elevation of temperature to 101 F and occasional hemoptysis Purplish nodules, the size of a small marble, are present on the extensor surfaces of the forearms, arms, thigh and face These nodules first appeared eighteen months ago

Tubercle bacilli were found in the sputum The urine contained albumin (1 plus) The Kahn reaction of the blood was negative A roentgenogram of



the chest showed a dense irregular round opacity between the sixth and ninth left ribs. The hematologic examination showed 12,000 leukocytes, with 80 per cent polymorphonuclears (40 per cent band forms), 7 to 8 per cent metamyelocytes, 6 per cent monocytes and 6 per cent eosinophils.

A histologic section was presented.

#### DISCUSSION

DR. MARCUS R. CARO: I thought that the sections showed the histologic changes of leukemia. I showed them to a general pathologist, and he thought that the eruption was some type of lymphoblastoma. I do not believe that this is a case of sarcoid.

DR. RUBEN NOMLAND, Iowa City: I think that this is a special type of aleukemic lymphatic leukemia in which there is enlargement of the lymph nodes, but no changes of blood. I have seen 4 or 5 such patients with enlarged lymph nodes in which cutaneous lesions developed without a leukemic blood picture.

#### Acrodermatitis Atrophicans Chronica and Squamous Cell Epithelioma

Presented by DR. THEODORE CORNBLEET and (by invitation) DR. HENRY C. SCHORR and DR. M. S. KAGEN

A 58 year old white woman has had an atrophic process of the extensor surfaces of both upper and lower extremities. The epitheliomatous lesion has been present on the back of the right hand for one year. The patient is presented to show the combination of atrophy and superimposed malignant changes.

A histologic section was presented.

#### DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Some authors classify acrodermatitis atrophicans chronica as a precancerous dermatosis. In a recent paper with Major R. R. Sullivan (*Acrodermatitis Atrophicans Chronica*, *ARCH. DERMAT. & SYPH.* 51:32-47 [Jan.] 1945), I pointed out that acrodermatitis atrophicans chronica is rarely associated with neoplastic changes and that development of epithelioma is usually coincidental and is associated with senile keratoses. This patient had received a severe trauma to her hand before the epithelioma developed. It is not uncommon to obtain a history of epithelioma following trauma or chronic indolent ulcers resulting from trauma. Acrodermatitis atrophicans chronica is not per se a precancerous dermatosis and should not be so classified.

DR. OLIVER S. ORMSBY: Some years ago I had a patient with a similar lesion on the back of the hand that followed a bite by a horse. That proved to be a squamous cell epithelioma. The only therapy in such a case is surgical removal. The lesion would be resistant to treatment with roentgen rays or radium. Dr. Mitchell photographed my patient, and the photograph is a counterpart of the appearance of the patient presented today.

DR. MAURICE OPPENHEIM (by invitation): The combination of epithelioma with acrodermatitis is extremely rare. In my article on "Atrophy of the Skin," in the *Handbuch* of Jadassohn, I mentioned only 1 case that had come under my observation among the many cases I observed. Sarcoma cutis seems to occur frequently in combination with acrodermatitis atrophicans, like the formation of fibromas, acrofibromatosis, which I was the first to describe in this disease. In the case presented today the biopsy specimen showed a squamous cell epithelioma on the right finger, but the patient had sustained a trauma to that finger. I do not believe that acrodermatitis atrophicans chronica is to be considered as a precancerous disease as it is the degenerative senile atrophy of the skin or that farmers' and sailors' skin, or the chronic roentgen ray or radium changes of the skin are to be so considered.

DR. H. E. MICHELSON, Minneapolis: I should like to emphasize that injury plays a part in the pathogenesis of cancer on the back of the hand. Dr. Bell,

pathologist of the University of Minnesota College of Medicine, in sectioning such a lesion, found a sliver of wood in the center. One must keep constantly in mind that such a cancer may be listed as an industrial risk.

DR L F WEBER. I have been interested in the subject for a long time and have been following the discussion in *The Journal of the American Medical Association*. Did trauma precede the lesion? I do not know how one is going to prove the point.

DR MAURICE OPPENHEIM (by invitation). Regarding cancer and repeated trauma, I agree with Dr Ormsby and Dr Michelson that this is a typical cancer with all the earmarks of a preceding trauma. The traumatic cancer originates on areas of the skin where it is exposed to repeated, frequent little injuries. I mention only the cancer on the temporal area where the bow of the spectacles is continually rubbing, or, much better known, the so-called *Schusterdaumenkrebs*, or "shoemaker's thumb cancer," described by Stahr, following the repeated, frequent injury to the right thumb, where the awl cuts the thumb when the shoemaker perforates the leather or cuts the leather with the paring knife, the right thumb stops the awl and the paring knife.

DR L F WEBER. That is not the type of cancer under discussion. The same thing occurs in the pitch industry.

**Dermatitis Venenata Due to Hair Dye** Presented by DR DAVID V OMENS and (by invitation) DR M S KAGEN

D E, a Negro woman aged 26, had her hair dyed black on Dec 16, 1944. No shellac or hair straightener was used. Twenty-four hours later the scalp and face became swollen, followed by oozing of the scalp. The eruption continued to become severer, the patient being unable to open her eyes on December 19.

#### DISCUSSION

DR L F WEBER. I think that the patient brings out one interesting fact. She said that a patch test was applied and that the reaction was negative, therefore, there is no value in administering patch tests to a patient never exposed to this hair dye.

DR J H MITCHELL. Are you in accord with Sulzberger's theory that one cannot be sensitized without being exposed to the drug itself?

DR L F WEBER. I am interested in this subject from the standpoint of the preemployment patch tests. I do not see that it is going to do any good if the patient has never been exposed to the different materials. I am willing to say that a material like mercury may give immediate response, but that is a different story. Suppose a new product should become available, I do not see any good in giving a patch test unless the person is exposed.

DR J H MITCHELL. What was the source of the paranitroaniline dye when it was put on the market?

DR L F WEBER. I do not know the source. During the last year dermatitis due to hair dye has become more frequent. I wonder whether any one knows the explanation. I have not come across the exact formulas. Here there is a Federal Trade Commission that is supposed to investigate these materials. They have physicians testifying and spending their time without much effect.

DR OLIVER S ORMSBY. In making a patch test most hairdressers put the dye on the back of the ear and wait for fifteen minutes, if there is no reaction then they go on with the dyeing. Dr Ebert and I have seen several patients with a severe dermatitis on the face, scalp and contiguous regions, including the area where the test patch was applied by the hairdresser. The hairdressers do not give the patch test which they use sufficient time to show whether or not the subject will react.

DR DAVID V OMENS The point which Dr Weber brought out is interesting. This patient had had a patch test, as I understood, of twenty-four hours' duration. On a negative reaction to the test the hairdresser proceeded to dye the hair. In twenty-four hours the woman came down with this dermatitis. I first saw her yesterday evening. The point I should like to bring up is that if hairdressers do not make a patch test and a dermatitis develops then they are liable.

**Hypertrophic Lichen Planus** Presented by DR DAVID V OMENS and (by invitation) DR M S KAGEN

T S, a white woman aged 71, suffered from gastric distress two years ago, and roentgenologic examination after a barium sulfate meal revealed a carcinoma of the stomach. Five months ago, shiny annular papules appeared on the dorsa of the hands, new lesions soon appearing on the extensor surfaces of the forearms, on the chest and neck and on the extensor surfaces of the legs. The eruption has improved during the past month while she has been in the hospital.

The histologic section showed lichen planus hypertrophicus.

#### DISCUSSION

DR DAVID LIEBERTHAL One does not find a generalized eruption in addition to hypertrophic plaques, except a scanty number of lichen papules in some cases and then as a rule near the plaques. I did not see the microscopic sections and would appreciate a description of these. Clinically I do not agree with the diagnosis.

DR DAVID V OMENS The histologic section showed lichen planus hypertrophicus—e g, there was a hyperkeratosis, the stratum granulosum was wanting, there was acanthosis with edema of the prickle cell layer and liquefaction necrosis of the basal cell layer, the papillae were elongated and edematous with dilatation of the blood vessels, and the uppermost portion of the corium presented a dense infiltrate composed of small lymphocytes which extended up into the papillae.

DR DAVID LIEBERTHAL How far did the infiltration go?

DR DAVID V OMENS Up into the summits of the papillae.

DR DAVID LIEBERTHAL In lichen hypertrophicus the cellular infiltration is not confined to the papillary and subpapillary layers but extends rather deeply into the corium. The epidermis shows considerable hypertrophy.

DR MARCUS R CARO I examined the section and thought the changes consistent with the diagnosis of lichen planus.

**A Case for Diagnosis (Rheumatic Nodules?)** Presented by DR THEODORE CORNBLEET

A P, a Negro woman aged 37, had a sore throat on May 15, 1944, followed by pain and swelling of the shoulder and hip joints, the thighs, knees and the leg. For the past six weeks pain and swelling have been present in the right forearm. Inflammatory nodules appeared subcutaneously on the flexor surface of the right forearm. The patient's temperature has remained elevated, at about 101 F. The throat is moderately injected, and there is a soft systolic murmur at the apex. The electrocardiogram showed a sinus tachycardia. A roentgenogram revealed that the chest was normal.

The sedimentation rate was 66 mm per minute. The tuberculin test elicited a strongly positive reaction in a dilution of 1:10,000. The urine was normal. The hematologic examination showed a hemoglobin content of 31 per cent, 3,200,000 erythrocytes, and 29,000 leukocytes, with a differential distribution of 79 per cent polymorphonuclears, 8 per cent lymphocytes and 13 per cent monocytes. The non-protein nitrogen level of the blood was 23 mg per hundred cubic centimeters.

## DISCUSSION

DR THEODORE CORNBLEET These lesions have almost completely disappeared since last week. There is little now on which to base a diagnosis, but my feeling was that these were rheumatic nodules.

**A Case for Diagnosis (Purpura?)** Presented by DR THEODORE CORNBLEET and (by invitation) DR DAVID COHEN and DR M S KAGEN

V K, a housewife aged 44, has had lesions on both legs for eight years. The patient dates the onset from a trauma of the left leg, which resulted in an ulcer. On both legs and ankles there are multiple lesions in various stages of evolution, one of them at the inner surface of the right ankle has a sharply outlined border, somewhat hemorrhagic in character. Its center is covered with scaly crusts. There are definite hemorrhagic and telangiectatic borders at the periphery which are sharply outlined. The lesions leave brownish stains with some atrophy. They are painful. The patient has difficulty in getting about and uses crutches. During her stay in the hospital, bullous elements were no longer seen.

Examination of the blood showed a hemoglobin content of 80 per cent and a differential leukocyte count of 70 per cent polymorphonuclears, 21 per cent lymphocytes, 8 per cent monocytes and 1 per cent eosinophils. The urine showed an occasional white blood cell and a small quantity of albumin. Determination of the blood chemistry showed a nonprotein nitrogen content of 37 mg, a glucose content of 75 mg and a total cholesterol content of 167 mg per hundred cubic centimeters. The basal metabolic rate was -11 per cent. The Kahn reaction was negative. The fluoroscopic examination of the chest showed no abnormalities.

## DISCUSSION

DR H E MICHELSON, Minneapolis By coincidence I have observed a patient in the last few weeks with lesions almost identical with these. When I first saw her, I thought that the diagnosis was either erythema multiforme or purpura. I believe now that the whole disease is on a purpuric basis.

DR THEODORE CORNBLEET The noteworthy thing about this eruption is its rapid and unpredictable changes. Today hemorrhage and vascularity are the keynotes, yet these have on other occasions been totally absent. Dr Ebert noted blisters at one time, and I have seen grouped vesicles followed by superficial crusts. There has been a play of suggestion between Majocchi's disease and necrobiosis lipoidica diabetorum, but the disease seems to be neither. Simple purpura with secondary changes may prove to be the final diagnosis.

**Keratosis Follicularis (Darier)** Presented (by invitation) by DR Z FELSHER and DR S ROTHMAN

A M, a white man aged 34, began to have "red pimples" on the chest six years ago, which persisted and gradually increased to confluent crusting areas. The initial lesion was described as a papule, which later became eroded, oozing and crusting. The involvement of the chest was followed by an eruption in the groins, in the axillas and on the abdomen, back, face and scalp. There is practically no itching and only slight burning. In recent years there has been but slight variation in the eruption, in spite of treatment elsewhere with intravenous injections of calcium salts, applications of ointments and ingestion of pills and capsules of unknown composition.

The examination reveals large reddish brown raised patches with yellowish greasy crusts on the areas mentioned. Near these patches single red crusted papules can also be seen. An offensive odor is present.

The laboratory examinations, including studies of vitamin A, have not yet been completed, as the patient was first seen in the University of Chicago clinics a few days ago.

The fluoroscopic examination revealed that the chest was normal. The Wassermann and Kahn reactions were negative.

## DISCUSSION

DR DAVID V OMENS: This is the first case of Darier's disease I have seen in which I thought I saw some inflammation of the mucous membrane around the gingival margin.

DR S ROTHMAN (by invitation): Involvement of the buccal mucous membrane was reported in several cases at the Eleventh International Convention.

NEW YORK ACADEMY OF MEDICINE, SECTION OF  
DERMATOLOGY AND SYPHILIS

Harry C Saunders, MD, *Chairman*

Frank Vero, MD, *Secretary*

Jan 2, 1945

A Case for Diagnosis (Melanoma of Skin?) Presented by DR CHARLES WOLF

I M, a man aged 51, has had for many years a flat pigmented lesion in the epigastric region, covering an area 3 by 4 cm. Pigmentation is lighter on the lower third and darker on the upper two thirds. In the latter section there are three raised rather firm nodules, the size of a split-pea, covered with a scale.

The Wassermann reaction of the blood was negative.

## DISCUSSION

DR MAURICE J COSTELLO: Therapy for malignant melanoma is discouraging as a rule, but wide surgical excision of the lesion with resection of lymph nodes would probably be the best approach.

DR DAVID BLOOM: Clinically, the lesion may be a benign pigmented nevus. In order definitely to ascertain the diagnosis a biopsy is necessary.

DR LOUIS CHARGIN: I am in favor of Dr Bloom's suggestion. It is difficult to obtain a good history from this patient. He says that he has had the lesion for a good many years, but whether it was nevus or is a new growth it is hard to tell. The lesion has become darker than it was originally, but it certainly does not show the clinical characteristics of a malignant melanoma. One should not hesitate to perform a biopsy in order to make certain of the diagnosis, but one should be prepared to perform a radical excision if the lesion turns out to be a melanoma.

DR GEORGE M LEWIS: I agree with Dr Chargin. I believe that the presence of a rough and irregular surface helps to distinguish the lesion from a true melanoma. The patient's history of having had the lesion all his life, with no change of recent date, is certainly in favor of a benign lesion. If biopsy is performed, the frozen section technic should be employed.

DR FRED WISE: I see no reason why one cannot perform a simple excision extending a quarter of an inch (0.6 cm) beyond the lesion, suture the edges of the wound and then study the histologic features. I think that there is no urgency whatever about the therapy. I believe that a simple operation is all that is necessary for a lesion of this kind and that wide and deep excision is contraindicated.

DR LOUIS CHARGIN: It has always been my practice to do as Dr Wise suggests—namely, when a lesion is amenable to surgical intervention and lends itself with ease to suturing this is the procedure I nearly always practice. How-

ever, the lesion which this patient presents is so located that it will be impossible to draw the skin together without tension. Therefore, I advise a biopsy first, then, if it proves necessary, a wide excision should be performed, followed by a graft.

DR OSCAR L. LEVIN: This type of lesion is always of great interest, first, because of the question of diagnosis and, second, because of its prognosis. It is frequently impossible to state from a cursory examination whether the lesion is malignant or benign. I have observed similar lesions which were apparently benign but which recurred after removal. On the other hand, a pigmented, verrucous, hypertrophic, growing lesion which suggests a malignant growth may be cured by the same method of treatment. I believe that this lesion is benign, but it should be thoroughly destroyed. As to the treatment of malignant cutaneous lesions, there is always great difficulty in knowing what to do. I perform as few biopsies as possible, but I remove the whole lesion without unnecessary trauma. In this case, after removal of the lesion, the skin may be drawn together or left open and allowed to heal by granulation. Growths suspected of being malignant should not be curetted for examination of tissue, but should be removed and sent for pathologic investigation, especially if thought to be melanocarcinoma. In this case I would give a favorable prognosis if the lesion is removed completely, either by surgical methods or by the cutting current. No form of therapy would be of avail if the lesion should prove to be a melanocarcinoma.

DR MAX SCHEER: Most of the men who have discussed this case assume that if the lesion is malignant it is a melanocarcinoma. I recently saw a man 70 years of age with a pigmented nevus which was proliferating. Biopsy was performed, and Dr. Sachs reported it as a beginning prickle cell epithelioma.

DR CHARLES WOLF: Performing a biopsy is impractical for a lesion of this sort, because one may cut a part of the tissue which shows no malignant changes, whereas in another part of the lesion there may be definite signs of malignancy. It is therefore of advantage to excise the entire lesion. Nothing is lost thereby, and added information is obtained. Furthermore, the prognosis is influenced by the entire elimination of the lesion. If it is found that the lymphatics and capillaries are infiltrated by malignant cells, the prognosis is grave with regard to ultimate cure. Statistics show that 30 per cent of all lesions of this kind are melanocarcinomas, which recur within two to five years after complete excision. Pack, of Memorial Hospital, who has had the greatest experience in number of patients treated, states that 14 per cent survive after five years. Therefore, complete excision is the treatment of choice on a part of the anatomy where it can be done. I presented to this society last year an old man with a nevocarcinoma or melanoma of the foot in which the question of amputation arose. The patient decided against it, and roentgen ray therapy was given with extremely good results. I feel that dilly-dallying with these lesions is not the proper approach. If the patient has any chance, it is by complete excision at the first sitting.

#### Necrobiosis Lipoidica Diabeticorum Without Diabetes Presented by DR HENRY SILVER

D. F., a woman aged 59, came to the dermatologic clinic of Mount Sinai Hospital on Aug. 29, 1944, complaining of lesions on the legs. There were no subjective symptoms, and the patient seemed to be otherwise in good health.

On the extensor surface of the right leg there is a large plaque about 2 inches (5 cm.) wide and 6 inches (15 cm.) long, well defined, parchment-like and tense. The central portion shows numerous telangiectases. The margin is brownish, and the center is reddish yellow. There are smaller lesions on the lateral aspect of the right leg and the dorsal surface of the leg, which are indurated and copper red with central healing. Some of the lesions show scar formation and others telangiectasia. The configurated lesion below the left knee shows a firm infiltrated brownish border with a central atrophic area. On diascopic pressure some of the lesions show a yellow, wax color.

Examination of the blood showed 88 per cent hemoglobin and 6,350 white blood cells, with 68 per cent segmented forms, 1 per cent nonsegmented leukocytes, 27 per cent lymphocytes, 3 per cent monocytes and 1 per cent eosinophils. The blood sugar level was 94 mg per hundred cubic centimeters on October 18 and 102 mg on December 31. Tuberculin tests elicited negative reactions with dilutions of 1:1,000, 1:10,000 and 1:100,000. The Wassermann reaction of the blood was negative. The urine was normal. Histologic examination showed changes compatible with sarcoid (reported by Dr P. Klemperer).

## DISCUSSION

DR DAVID BLOOM. It seems strange to me that of the many cases of necrobiosis lipoidica which I have observed personally or which I have seen presented at meetings diabetes was found in only a few. The histologic structure of sarcoid, together with tuberculin anergy, justifies the diagnosis of sarcoid. A study of the lungs and bones is indicated.

DR FRED WISE. Although some parts of the eruption closely simulate both scleroderma and sarcoid, I regard the eruption to be necrobiosis lipoidica, despite the histologic report. Disseminated sarcoid strictly confined to the legs is a possible diagnosis but an extremely unlikely one.

DR MAURICE J. COSTELLO. I think that the patient has necrobiosis lipoidica. In sarcoid there is usually no scarring, which this patient does show in the center of the lesions. I think that the color is redder than is usual for necrobiosis lipoidica, but the play of color from red to yellow seen in that dermatosis is present.

DR PAUL GROSS. The histologic changes of sarcoid bear out the diagnosis of necrobiosis. These sarcoid-like changes have been described by several authors, and I have seen such cases with a microscopic picture very difficult to distinguish from that of sarcoid. Clinically, I think that there is no doubt of the diagnosis of necrobiosis.

DR LOUIS CHARGIN. I should like to join those who think that it is necrobiosis and not sarcoid for the following reasons. The sex of the patient and the location of the eruption are points strongly in favor of necrobiosis instead of sarcoid. The character of the lesions is also in favor of necrobiosis, the scleroderma-like lesions with raised borders, the play of colors and, lastly, the histologic picture, all favor necrobiosis. As Dr Gross has stated, a sarcoid-like histologic structure has been found frequently in necrobiosis. Diabetes is found in 70 per cent of the cases.

DR CHARLES MILLER. I agree with the clinical diagnosis of necrobiosis lipoidica. The microscopic picture of sarcoid is different from that of necrobiosis lipoidica. In sarcoid there are naked tubercles, singly or in grouped masses of epithelioid cells with little cellular reaction about them. In necrobiosis there is a cellular reaction composed of epithelioid cells, round cells and wandering connective tissue cells about a central area of necrosis. In an old lesion of necrobiosis the cellular reaction about the necrotic zone may be composed almost entirely of epithelioid cells, with an occasional or many giant cells. This necrotic zone in the center is not seen in sarcoid. The report of sarcoid-like structure to me means a cellular reaction in which there is a predominance of epithelioid cells. This does not make the histologic diagnosis of sarcoid. With the features previously noted, the histologic diagnosis of necrobiosis lipoidica can be made.

DR FRANK VERO. Several years ago I presented a patient from the Vanderbilt Clinic with the clinical picture of scleroderma, in which the histologic picture showed a sarcoid-like structure (A Case for Diagnosis Tuberculous Granuloma (?), ARCH DERMAT & SYPH **29** 453 [March] 1934). Another similar case was presented from the Lincoln Hospital, in which the lesions resembled both scleroderma and necrobiosis (Sarcoid, Sclerodermatiform Tuberculous Type (Gougerot), ARCH DERMAT & SYPH **37** 895 [May] 1938). In the discussion Dr Traub mentioned similar observations. In the *Handbuch* several other cases have been cited as having been described by Gougerot as sclerodermatiform sarcoids.

If the lesions below the knee in this case were seen on the face, I think that one would not hesitate to make a diagnosis of sarcoid. I feel that further histologic studies are necessary in order to rule out sarcoid.

DR HENRY SILVER: I agree with those who regard the case as one of necrobiosis lipoidica. Dr Bloom and others feel that the lesions are more suggestive of sarcoid. Dr Miller states that if the lesion below the knee were seen on other parts of the body—for example, on the forehead—he would not hesitate to diagnose it as sarcoid. To my mind, the lesion below the left knee, which shows changes seen in morphea, is clinically characteristic of necrobiosis. It has been stressed by Oppenheim that in some cases atrophy is a salient feature, and before Urbach penned the name “necrobiosis lipoidica diabetorum” Oppenheim suggested the name “dermatitis atrophicans lipoidica diabetorum.”

Before dermatologists became familiar with this disease, cases of this type were regarded as instances of localized scleroderma. Some of the members will recall the case presented before this section by Dr Gross as one of morphea with xanthomatous changes, later diagnosed as necrobiosis lipoidica (ARCH DERMAT & SYPH 30 598 [Oct] 1934).

I fully agree with Dr Chargin's clinical analysis of the case. Also in favor of necrobiosis is the observation made by Dr Wise, namely, that no case of sarcoid has been observed in which the eruption is strictly limited to the legs. These features, the clinical character of the lesions with the glazed appearance, telangiectasia and atrophy and the atypical histologic picture strongly suggest necrobiosis lipoidica.

As to nomenclature, Dr Bloom's point is well taken. Too many cases of necrobiosis in nondiabetic patients are on record to warrant the inclusion of the descriptive but misleading term “diabeticorum.”

#### Xanthelasma Presented by DR JACK WOLF

J G, a man aged 76, is presented from the dermatologic clinic of the Mount Sinai Hospital, with an eruption of two years' duration. There was nothing unusual in his past history except that some fifteen years previously he had contact with aniline dyes in the course of his occupation.

The patient presents a rather unusual and striking picture, with diffuse yellowing of the neck, the upper aspect of the chest and the shoulders. The eruption is flat, nonelevated and not thickened. On the upper and lower lids the eruption is more localized, here it is elevated and extends in rimlike fashion by coalescence over the inner and outer canthi. The yellowish infiltration is widely distributed over the face but occurs chiefly in strands along the folds of the skin on the forehead, cheeks and chin.

The blood sugar level was 89 mg per hundred cubic centimeters. The serum albumin content was 2.8 Gm, serum globulin 2.2 Gm and total protein 5 Gm per hundred cubic centimeters. The urea nitrogen was 18 mg and the cholesterol level 210 mg per hundred cubic centimeters, of which 160 mg was esterified forms. Biopsy was reported as indicating xanthomatosis.

#### DISCUSSION

DR MAX SCHEER: This is the most extensive case of xanthelasma that I have ever seen, and I should not be surprised if it were the most extensive on record.

DR PAUL GROSS: It is known that xanthelasma of the eyelids is simply xanthoma. It has nothing to do with degeneration of muscle fibers. This is a case of extensive xanthoma, the unusual feature being the distribution, especially over the neck. The distribution may remind one of pseudoxanthoma elasticum, and, despite the age of the patient, this disease should be ruled out.

DR JACK WOLF: The eruption resembling pseudoxanthoma elasticum on the neck has no bearing on the extensive superficial xanthelasma eruption on the face.



and chest. The unusually extensive sheetlike character of the eruption, I felt, warranted the presentation.

#### **Acanthosis Nigricans (Juvenile)** Presented by DR JACK WOLF

G I, a Negro girl aged 14, is presented from the dermatologic clinic of the Mount Sinai Hospital, with an eruption on the chin, neck and intermammary region of one year's duration. The eruption appeared suddenly and assumed its present form within a relatively short period.

The greater part of the neck is covered with deep black, transverse, linear, hypertrophic strands, approximately  $\frac{1}{16}$  of an inch (0.16 cm) in width, separated by furrows whose bases represent normal cutaneous markings. In the intermammary region the strands are neither as elevated nor of the same deep black color—assuming a brownish black hue—as they are on the chin and the neck. The anterior aspect of the chin is erythematous and dry and imparts a sense of roughness to the touch. The surrounding zone is hyperpigmented.

Except for pronounced obesity, physical examination revealed no abnormality.

The blood count and the results of a sugar tolerance test were normal. The blood calcium level was 7.1 mg and cholesterol 300 mg per hundred cubic centimeters. The basal metabolic rate was  $\pm 0$ . A roentgenogram of the skull showed the sella turcica to be normal. Roentgenologic studies of the gastrointestinal tract revealed no abnormalities.

Histologic examination showed hyperkeratosis, acanthosis alternating with areas of atrophy of the prickle cells, striking pigmentation of the basal layer and absence of *corps ronds*. It was felt that this conformed with acanthosis nigricans.

#### DISCUSSION

DR HELEN O. CURTH: The beginning of the cutaneous lesions dates back two years, to the time when the patient began to menstruate. In about 50 of the reported cases the cutaneous lesions developed at the time of puberty. Children either are born with acanthosis nigricans or show the first lesions in early childhood or at puberty. As to the prognosis, I think that the disease in this case has every chance to remain benign, that is, there may be some spreading of the cutaneous lesions or some regression in the next few years, without the rapid spreading and intensification of these lesions paralleling the course of accompanying cancer which characterize the malignant form. While one may say cautiously that cases in which cutaneous lesions develop long after puberty are all cases of the malignant type, the reverse is not true. A few persons with the malignant type have been found among those in whom the lesions developed in childhood or during puberty.

DR FRED WISE: I agree with the diagnosis.

DR CHARLES WOLF: It seems worth while to me to investigate the case further. The patient has stigmas which indicate that the adrenal glands or one of the endocrine glands is affected. I should therefore like to be certain that hypernephroma or Wilms's tumor is eliminated. On the strength of that I suggest further roentgenographic study and also pituitary examination. In such cases malignancy of either or both of those glands sometimes appears later.

DR JACK WOLF: This patient has been studied thoroughly. Roentgenologic examination revealed that the skull is normal. An attempt will be made to carry out the suggested study of the kidneys.

#### **Pustular Psoriasis (?) Treated with Penicillin Ointment** Presented by DR HENRY SILVER

H T, a man aged 52, a barber, is presented from the department of dermatology of the Mount Sinai Hospital. He has been suffering from an eminently chronic recurrent eruption involving the hands and feet for the past fourteen years. He states that at intervals he has been completely free of the eruption. Being a barber,

the patient necessarily comes into frequent contact with hair lotions, shampoos, etc. In 1934 he was treated at the clinic of Mount Sinai Hospital with a variety of ointments and roentgen rays without appreciable benefit. In 1940 he was seen at the dermatologic clinic of the New York Hospital. At that time he showed erythematous scaly lesions with some thickening on the soles and outer sides of the feet. There was little scaling between the toes. The palms were reddened, slightly thickened and scaly. A few discrete pustules were scattered over this area. The impression was that the patient was suffering from pustular psoriasis.

The last episode began in October 1944, involving chiefly the hands. The palms, and especially the ulnar sides, showed densely set vesicular and pustular lesions the size of a pinpoint or pinhead. The sides of the fingers were similarly involved. The soles showed circumscribed quarter-sized scaly patches. Scaling and slight maceration were seen between the toes. Cultures were negative for fungi.

On December 19 an ointment containing 500 units of penicillin per gram was prescribed. One week later only a few pustules were present on the palms. Most of the lesions dried and began to desquamate. The eruption has since considerably improved.

Histologic examination revealed parakeratosis, absence of the stratum granulosum, thinning of the suprapapillary portion of the epidermis and widening and thickening of the interpapillary portion of the epidermis. Focal spongiosis and vesiculation with a few polymorphonuclear leukocytes were seen. The picture was that of psoriasis, but no conspicuous microabscesses were found.

#### DISCUSSION

DR DAVID BLOOM: This is probably a case of pustular psoriasis. Whether penicillin can be considered to be beneficial for this disease can be determined only from observation of its effect in many cases of pustular psoriasis. Improvement may be infrequently observed following application of boric acid ointment. In the past few months I have found Goeckerman's treatment of psoriasis to be beneficial also in treating pustular psoriasis.

DR FRED WISE: I admit the possibility that the patient has pustular psoriasis, but there is no direct evidence to that effect. It has been my practice not to diagnose palmar and plantar eruptions as pustular psoriasis unless there is evidence of psoriasis—past, present or future—on other parts of the body. It is hazardous to make that diagnosis without corroborative lesions. The results of penicillin therapy are interesting, but they do not affect the diagnostic problem.

DR GEORGE M. LEWIS: I agree with Dr. Wise that in many cases it is possible to make a diagnosis of pustular psoriasis without finding lesions on other parts of the body. I should like to call the attention of the members to the cases presented at the October meeting in which Dr. Frederick Reiss pointed out the value of intravenous injections of antimony and potassium tartrate in the treatment of the disease. Since then additional cases with this treatment have been followed and it does seem to be a worth while procedure. The drug must be given with care and the patient watched for reactions. Penicillin has not been too successful in the treatment of virus diseases. It may be just a coincidence that there has been improvement in this case.

DR PAUL GROSS: I am afraid that the issue is being somewhat obscured. First of all, the society should go on record as saying that there are two diseases. The one is pustular psoriasis, which may begin with vesicles but in which sooner or later lesions typical of psoriasis develop, and the other has rightly been put by Andrews under the heading of pustular eruptions of the palms and soles. Some of these eruptions may be cleared successfully by the removal of the foci of infection, but I do not know of any psoriasis which will respond to such methods. One must distinguish between those two groups. If there is an eruption on the palms and soles and if there is response to a sulfonamide ointment or penicillin, I should be inclined to consider the disease a local streptococcal infection. Even in the case of bacterid one may get a response with an antiseptic ointment. On the other hand, if one wants to prove the response of psoriasis, why not take a patient

with typical psoriasis and administer penicillin? Many patients with psoriasis ask whether they should use a sulfonamide ointment. Pustular psoriasis, if investigated, will show many features of psoriasis, including a hypercholesteremia, and in my hands it has responded to soybean phosphatides. I think that in order to differentiate between the two diseases one must go a little further than giving them a name.

DR HENRY SILVER: I appreciate Dr Wise's strict criteria for establishing a diagnosis of pustular psoriasis. In spite of the points in favor of this diagnosis, I still hesitate to regard this case as one of definite pustular psoriasis and I therefore stressed the occupational element. The patient is a barber and frequently comes into contact with alkalis, hair tonics, shampoos and other materials, which conceivably played a role in the recurring episodes during the fifteen or sixteen years he has suffered from the eruption.

As regards the penicillin ointment, it contains 500 Oxford units per gram, made up in a greaseless base. I do not want to convey the impression that penicillin ointment cured pustular psoriasis. I am simply submitting this case as one of a series of cases of dermatoses in which the local action of penicillin is being studied. Only two weeks ago the patient presented an acute vesiculopustular eruption, with numerous lesions on the palms. The eruption responded favorably and rapidly to the treatment.

#### **Sycosis Vulgaris Treated with Penicillin Ointment** Presented by Dr HENRY SILVER

H L, a man aged 55, came to the dermatologic clinic of the Mount Sinai Hospital on April 4, 1944, presenting an eruption limited to the upper lip, of four months' duration. The patient had been treated previously at the surgical clinic for a localized cellulitis of the tip of the nose. From April until May 15, 1944, he was treated successively with ointments containing chlorohydroxyquinoline, sulfathiazole and ammoniated mercury, without benefit. From May 15 to 31 he was given three exposures (75 r each) of unfiltered roentgen rays. The eruption failed to respond to treatment. On November 30 the eruption was limited to the left side of the lip. The involved area was erythematous and edematous and studded with pinhead-sized pustular lesions. Some of these dried, forming superficial yellowish crusts. An ointment containing 500 Oxford units of penicillin per gram was prescribed. By December 16 the improvement was striking. The patient began to shave daily. One week later the eruption had completely cleared.

#### **DISCUSSION**

DR MAURICE J COSTELLO: I did not see the patient, but I should like to bring up a point. The eruption of sycosis vulgaris apparently does not respond completely to the intramuscular injection of penicillin, but it is favorably influenced by penicillin ointment, 500 units per cubic centimeter of vehicle.

DR CHARLES WOLF: I am sure that Dr Silver does not want to convey the impression that sycosis vulgaris is going to be cured by the application of penicillin. This patient has had many attacks of the disease, which is a recalcitrant dermatosis that improves with a variety of treatments. Only a year ago I treated him for a pronounced lymphangitis accompanying the sycosis of the upper lip. It cleared with topical applications. One can learn the effect of penicillin ointment by observing the length of time this man remains free of symptoms. It is rather early now to draw conclusions, a week after apparent involution. It would be worth while to have a few cases presented at some future time, after observations have extended over a longer period.

DR LOUIS CHARGIN: I have had experience in treating 3 patients having sycosis with penicillin ointment, all of them previously treated with other remedies, such as roentgen rays and antiseptic ointments including chlorohydroxyquinoline ointment, with reasonable success for long periods but always followed by recur-

rence I can now report equally good results from penicillin ointment, in 1 case after one month and in the 2 others after two weeks each. However, I know full well that it is impossible to speak of a cure in any case of this disease without prolonged observation. One patient, in whom atrophy of the skin developed following roentgen ray treatment and who, in addition, had active lesions for almost a year, has been considerably improved after four weeks of treatment with penicillin ointment.

DR FRED WISE: Have there been any reactions?

DR LOUIS CHARGIN: None of the 3 patients whom I treated have had reactions.

DR HENRY SILVER: My impression is that penicillin applied locally is of considerable value in sycosis vulgaris. The patients I have observed for the past few months have shown decided improvement. This patient responded rather rapidly to the treatment. He has been under my care for over a year, and all attempts to influence the condition failed. The eruption was extremely resistant and flared up frequently. Four weeks ago before penicillin therapy was begun, the upper lip was considerably swollen and studded with pustules. Within ten days the inflammation subsided and then cleared. Dr. Rosen, who observed the patient while he was under treatment, was surprised at the rapid involution. I agree with Dr. Costello that the local action of penicillin is apparently specific for sycosis vulgaris while penicillin by the intramuscular route does not influence the disease.

#### **Pityriasis Lichenoides et Varioliformis Acuta** Presented by DR ISADORE ROSEN

H. K., a man aged 35, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with a generalized eruption of six weeks' duration. The eruption consists of reddish round slightly infiltrated lesions, measuring about 5 mm to 7 mm in diameter, most of which show a scaly collaret at the periphery or are covered with a thin crust or scale. The eruption is more profuse on the flanks than on the back and the abdomen but is particularly profuse on the anterior and posterior aspects of the extremities. There is also involvement of the palms and soles and of the glans and sulcus coronae of the penis. The face is free of lesions. The eruption appeared six weeks ago on the right thigh, and within a week it spread all over the body. There is mild pruritus.

General examination revealed a slight enlargement of the inguinal lymph nodes as the only abnormality.

The Wassermann reaction of the blood was negative.

#### DISCUSSION

DR LOUIS CHARGIN: I expressed the opinion at another meeting that this was not a case of secondary syphilis, even though the eruption bore a close resemblance to that disease. Subsequently, I again had occasion to examine the patient and confirmed my first impression that one was not dealing with syphilis, particularly in view of the vesicular lesions present on the palms.

DR DAVID BLOOM: The fact that this patient's face is entirely free of lesions, in contradistinction to the patient with secondary syphilis who shows a profuse papular eruption on the face, points also to the diagnosis as presented.

DR MAURICE J. COSTELLO: This patient complains of severe itching, which also is not present in secondary syphilis.

#### **A Case for Diagnosis (Mycosis Fungoides?)** Presented by DR ISADORE ROSEN

A. E., a woman aged 69, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with a generalized eruption of three years' duration, involving the face, trunk and extremities. Severe

pruritus is present. The eruption consists of infiltrated raised coin-sized red lesions which in most places have coalesced to form large plaques. On the abdomen the lesions are discrete and moderate in number.

General examination revealed enlarged axillary lymph nodes. Biopsy was reported as indicating only "dermatitis." The blood and differential counts were as follows: hemoglobin, 77 per cent, erythrocytes, 3,540,000, and leukocytes, 8,920, with 51 per cent polymorphonuclear leukocytes, 27 per cent eosinophils, 13 per cent lymphocytes and 9 per cent monocytes. The color index was 1.1.

#### DISCUSSION

DR OSCAR L. LEVIN: When the patient was examined at Mount Sinai Hospital she showed an acute, generalized, almost universal dermatitis. I attributed the eruption to an external agent, possibly hair dye. However, the eruption persisted, resisted local treatment and after several months showed infiltration. During the past two years the infiltrations have become more pronounced, and tumor-like structures have developed. Lesions of this type may represent an allergic reaction of the skin with possible development of tumors made up of eosinophils, as I have observed in a case of dermatitis herpetiformis. This evening the skin showed areas which were white and apparently normal, while in other spots there were elevated lesions suggesting mycosis fungoides.

DR JACK WOLF: This patient has had numerous biopsies, all with the histologic picture of chronic dermatitis. I favor the diagnosis of chronic lichenoid and discoid exudative dermatitis. The exudative lesion is predominant, but I do not believe that either this feature or the sex of the patient militates against this diagnosis.

DR FRED WISE: I still believe that the patient is a candidate for mycosis fungoides. All dermatologists know that this disease is sometimes preceded by an eczematous dermatitis with a histologic picture showing nothing specific, and as time goes on the eruption may become transformed into mycosis fungoides. Dr. Wolf says that there is no reason to assume that exudative and discoid lichenoid dermatitis does not occur in females; I have never seen it in a female, though that does not say that it does not occur. In this case one has to take into consideration the fact that there are definite nodules and tumor-like formations on the arms. On the hand the patient has a frambesiform lesion about the size of a dollar, which has the clinical appearance of a granuloma. I should like to ask whether roentgen ray therapy has been attempted and, if so, what change it produced in the eruption.

DR MAX SCHEER: I have also had an opportunity to follow this case for two years at Mount Sinai Hospital. One of my reasons for feeling that it is not a case of chronic lichenoid discoid dermatosis is that the clinical picture has been stationary during these two years, whereas in chronic lichenoid discoid disease the picture changes from time to time, sometimes resembling eczema, sometimes lichen planus and sometimes neurodermatitis or urticaria. This picture has remained unchanged, and although there is no histologic evidence I am of the opinion that this patient in all probability has mycosis fungoides.

DR PAUL GROSS: I was unable to examine the patient while she was undressed. Was there any enlargement of lymph nodes? In the absence of massive lymphadenopathy I should be against a diagnosis of lichenoid discoid exudative dermatosis. I agree with Drs. Rosen and Wise that this patient may eventually show a typical picture of mycosis fungoides.

DR GEORGE M. LEWIS: This patient was under my observation for only a short time, and my studies did not contribute anything to the further diagnosis of her case. My clinical impression was that she is a candidate for mycosis fungoides, based on the duration, the intense pruritus and the infiltrative type of lesion to be seen.

## MANHATTAN DERMATOLOGIC SOCIETY

George M Lewis, M D, *President*Wilbert Sachs, M D, *Secretary*

Jan 9, 1945

**Localized Scleroderma and Calcinosis Cutis** Presented by DR FRED WISE

G E, a man aged 42, in excellent general health, presents a tumor-like mass over the lower portion of the right scapula, which he first noted, about a month ago. The affected area is about 4 inches (10 cm) in diameter, slightly elevated above the surrounding skin and somewhat inflamed in the central portion, which is more prominent than the surrounding tissues of the plaque. To the palpating finger, the degree of induration is that of a hard rubber ball. The skin over the tumor mass is firmly bound down and has the clinical features of scleroderma. The biopsy punch encountered tissue which cut like gristle. Pain and tenderness are absent.

Histologic examination did not reveal sufficient changes to establish a definite diagnosis but indicated the existence of scleroderma with deposits of calcium in the corium.

## DISCUSSION

DR E WILLIAM ABRAMOWITZ I accept the diagnosis in this case.

DR VAN ALSTYNE H CORNELL (by invitation) The man stated that the eruption has been better in the last few days and that he has had it for only three or four weeks. I am wondering whether that was an accurate statement.

DR DAVID BLOOM In the cases of calcinosis which I have seen there were lesions over the joints—the elbows, knees and fingers. I favor the diagnosis of possible scleroderma in this case.

DR MAURICE J COSTELLO I think that the patient has localized scleroderma. The lesion is not hard enough to be circumscribed calcinosis, and the duration would certainly be unusually short for the evolution of a lesion of cutaneous calcinosis, in my experience. I studied 1 such patient carefully, and I think that it takes many months for nodules to form. Also, as Dr Bloom mentioned, they are all located over the joints.

DR WILBERT SACHS I thought that it was a case of scleroderma. Of course, it is always possible that calcium will be deposited in scleroderma. One would not need much tissue to see calcium if it were calcinosis. The sections would be difficult to cut.

DR MAX SCHEER I also feel that it is scleroderma.

DR HERMAN SHARLIT A diagnosis of calcinosis, to be justified, would permit no question in the mind of the pathologist. Just cutting the tissue with a knife is sufficient to reveal deposits of calcium salts. If there is any doubt that it is not a case of calcinosis I suggest that sections be sent to the laboratory for quantitative determination of the calcium present.

DR GEORGE M LEWIS There is one other possible diagnosis, and that is scleredema. This lesion is not in a location usual for scleroderma, and the lesion impresses me as showing edema rather than sclerosis. When I questioned the patient, he said that he had had the lesion for only three or four weeks, but this was indefinite. He just happened to feel it, and it was then about the same size as it is tonight, he thinks that there has been no change in the last little while. Calcinosis cutis is the last disease I should consider, and I am at a loss to understand why it is even mentioned.

DR FRED WISE The patient has no definite knowledge of the duration of the lesion, but he is sure that it was not preceded by an injury. When the specimen for biopsy was taken the tissue gave the impression of sectioning cartilage. Although microscopic examination failed to demonstrate calcium in the tissues,

it is possible that it was missed and that biopsy of another area would reveal its presence

**A Case for Diagnosis (Pseudoxanthoma Elasticum [?] in an Albino Negro Woman)** Presented by DR DAVID BLOOM

E S., a Negro woman aged 38, has had universal albinism all her life, except for a small number of brown spots, some of which are spider-like, on her face, neck and chest. The irises of the eyes are light brown and the pupils dark. The hair is reddish.

Besides albinism the patient presents other defects. The eyes show horizontal nystagmus, and the vision is defective (10/200). The patient suffers from photophobia. The palms, and more especially the soles, are hyperkeratotic. Both legs show pronounced nonpitting edema. The skin on the back of the wrists is thickened and shows accentuation of the lines. The skin of the neck shows a yellowish tinge, is considerably thickened and shows accentuation of the lines.

The patient's daughter is 10 years old and normal in color and other respects. The patient is one of fourteen children. Four siblings, three of whom are alive, were also albinos. The parents are both black, but the mother's father, aunt and uncle were albinos. Several paternal uncles and aunts were albinos.

DISCUSSION

DR FRED WISE I agree with the diagnosis as presented.

DR MAURICE J COSTELLO I did not get the impression that this patient had xanthoma elasticum, because one could not pick up the skin. In pseudoxanthoma elasticum one can "tent" the skin between the fingers. This patient has accentuation of the normal markings of the skin, but it is not thrown up into folds. The history of the case was most interesting because of the fact that there were several other albinos in the same family.

DR MAX SCHEER I think that this is a senile, or rather, presenile form of degeneration of elastic tissue such as is sometimes seen in younger people and in sailors, farmers and persons much exposed to ultraviolet rays and such as one would expect to find in this patient, who has no pigment to protect the skin. I do not think that the disease is pseudoxanthoma elasticum.

DR HERMAN SHARLIT I, too, am impressed by the fact that skin of that type is seen in farmers, sailors and in aging people, however, histologic study of the area should clear any doubts.

DR GEORGE M LEWIS The skin in the cubital fossae might be compared with the skin on the side of the neck for looseness or coarse wrinkling. I did not see lesions to support Dr Bloom's diagnosis.

DR DAVID BLOOM I intend to have an ophthalmologist examine the patient's eyes. As brought out in the history, there are several albino members in the families of both parents. Among twelve children, five were albinos, one of whom is the patient presented tonight. As albinism is a recessive trait, one would expect one fourth of the offspring to be affected, or three instead of five.

**Paget's Disease of the Nipple** Presented by DR MAURICE J COSTELLO

M B., a woman aged 49, a private patient, has had an eruption confined to the nipple and areola of the left breast for three years. It began around the left nipple and spread by peripheral extension. The patient states that a "sore" would form and heal, only to recur.

The eruption never disappeared at any time. About twenty-five years ago the patient had an abscess of the left breast which was incised above and below the present lesion.

The eruption is erythematous, sharply circumscribed, raised, shiny and infiltrated. There is no regional adenopathy.

## DISCUSSION

DR VAN ALSTYNE H CORNELL (by invitation) I thought that the eruption was an eczematous process. It appeared superficial to me. I felt no induration or tumor-like condition. I have observed only a few cases, but I have always felt a tumor underneath the nipple.

DR MIHRAN B PAROUNAGIAN Unless the disease is confirmed by biopsy, I would regard it as eczema rather than Paget's disease. It is superficial and eczematous in appearance.

DR DAVID BLOOM The fact that the eruption occurs on one breast only should make one suspect Paget's disease. A biopsy is necessary in order to be certain of the nature of the lesion.

DR JACK WOLF I think that this may well be a case of Paget's disease. Radical mastectomy is indicated.

DR WILBERT SACHS I believe this is a case of Paget's disease, but if it should be one of eczema there are malignant changes setting in. I advise mastectomy but not the radical procedure.

DR MAX SCHEER Some years ago I presented a patient with similar, but less extensive, lesions. In that case a biopsy specimen was taken about  $\frac{1}{2}$  inch (1.2 cm) to the side of the nipple and was reported as indicating eczema. A subsequent specimen, taken directly through the nipple area, showed definite cancer. I suggest that biopsy be made of a specimen taken directly through the nipple area. This history, the character of the lesion and its unilateral location, all point definitely to Paget's disease, and if this is confirmed I think that mastectomy should be sufficient.

DR HERMAN SHARLIT I completely endorse everything Dr Scheer just said.

DR FRED WISE Biopsy must determine the diagnosis. I think that the clinical manifestations and the history are strongly in favor of Paget's disease.

DR E WILLIAM ABRAMOWITZ I agree with the diagnosis of Paget's disease of the nipple. I am of the belief that Paget's disease of the nipple is a manifestation of cancer of the mammary duct—not a lesion that begins outside and extends inside, but one which begins in the breast. Weeping is not as important a clinical symptom of Paget's disease of the nipple as a persistent ulceration. With the patient on the table, a section should be taken and examined, and if it proves to be carcinoma amputation of the breast is in order. I have followed that course in several cases with good results, whereas if one waits until the lump is felt I think that it is too late.

DR WILBERT SACHS Paget's disease may start in the epidermis or it may start in the ducts, or in both at the same time.

DR MAX SCHEER May I take exception to Dr Sachs's statement? I was under the impression—not through personal experience but from the literature—that in all these cases the disease begins as intracanalicular cancer and involves the skin secondarily and that this is what is called epidermal Paget's disease. If biopsy were performed deep into the breast, intracanalicular carcinoma would probably be found.

DR JACK WOLF I should like to know why simple mastectomy is favored instead of radical excision for a process going on for three years, which more than likely started within the breast tissue.

DR MAURICE J COSTELLO I think that this case lacks nothing in the clinical sense to prevent it from being a classic case of Paget's disease of the nipple. Everything that one would outline to students is present. One important point is that this lesion has never receded, never improved, never disappeared and always extended. I am inclined to agree that it is intracanalicular, because most of these lesions begin at the nipple and spread from that point. It is interesting to observe the sharp line of demarcation between the tumor and the normal skin on transillumination.



**A Case for Diagnosis (Lupus Erythematosus, Tuberculosis?)** Presented by DR E WILLIAM ABRAMOWITZ

R P, a Negro woman aged 30, came to the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct 23, 1944, with an eruption of two years' duration on the face

On the left side of the nose near the canthus of the eye there is a nickel-sized, slightly raised strongly hyperpigmented, hyperkeratotic plaque with an uneven surface. A similar lesion, but half as large, is present on the left side of the upper lip

General examination revealed nothing essentially abnormal, except for some involuntary movements of the head for which the patient was referred to the neurologic department

A blood count revealed a moderate anemia. The sedimentation rate was 24 mm. The Wassermann and Kahn reactions of the blood were negative. A roentgenogram of the chest showed extensive old calcification of the hilar nodes. Biopsy of both lesions was reported as showing possible tertiary syphilis. Tuberculin in a dilution of 1:10,000 elicited a 1 plus reaction

From July to August, 1944, the patient received eight injections of ophthalmarsine hydrochloride without any influence on the lesions. Following four weekly injections of gold sodium thiosulfate in the total amount of 110 mg, the lesions showed moderate involution

## DISCUSSION

DR MIHRAN B PAROUNAGIAN I am in favor of a diagnosis of tuberculosis rather than of lupus erythematosus

DR DAVID BLOOM Both diseases may look alike in a Negro. Cutaneous tuberculosis in the Negro is known to assume many different appearances. The 2 cases reported by Dr Mendelsohn and me have been diagnosed at the various societies as cases of lupus erythematosus, tuberculosis or syphilis. Of the two suggested diagnoses I favor lupus erythematosus

DR MAURICE J COSTELLO I favor a diagnosis of lupus erythematosus of the hyperkeratotic type. The duration and the fact that there are two lesions instead of one suggest that diagnosis rather than lupus vulgaris

DR JACK WOLF I agree with the remarks made by Dr Costello

DR WILBERT SACHS Microscopically, the granulation tissue and the pure plasma cell reaction would rule out a diagnosis of lupus erythematosus. There are no giant cells and no tubercles, which would eliminate a diagnosis of tuberculosis. To me the disease is suggestive of syphilis

DR HERMAN SHARLIT I think that one should consider the fact that in colored skins the pigment at times is so great that it is impossible to be sure of any clinical diagnosis. If a biopsy report is presented in which evidence of the tuberculous group is distinctly absent, I think that it is only fair to accept this biopsy report and to rule out what the report says cannot be there. Sometimes the reverse is true, and the biopsy report needs interpreting in the light of clinical evidence. Here, however, the clinical picture is confused, and clinical judgment should carry little weight

DR FRED WISE I favor the diagnosis of lupus erythematosus

DR VAN ALSTYNE H CORNELL (by invitation) The disease did not look to me like lupus erythematosus clinically, but more like lupus vulgaris or syphilis. However, if it were the last it should have responded to antisyphilitic treatment. As I remember, the history said that administration of gold caused some improvement, hence I do not know what diagnosis to make. Clinically, I thought that the disease was syphilis

DR E WILLIAM ABRAMOWITZ Allowing for the peculiarities of tuberculosis in Negroes and not having a definite statement on the pathologic changes, of course I am more in favor of lupus erythematosus, knowing that Negroes have not only

peculiar types of tuberculosis of the skin but also peculiar types of lupus erythematosus. That opinion is based on my experience with several cases in which lupus erythematosus was not suspected even after histologic examination but proved to be cases of that disease after clinical and microscopic study.

### Edema of Eyelids and Cheeks on Exposure to Wind and Cold, Physical Allergy Presented by DR MAURICE J COSTELLO

A woman aged 32 came to the clinic complaining of redness and swelling of the eyelids and cheeks. She stated that she had had similar attacks for the past three years when she exposed herself to cold or windy weather. The eruption could not be produced by cold water. There was no swelling of the hands or fingers when they were allowed to remain immersed in cold water. Ethyl chloride was sprayed on the chest for several seconds, an area of redness appeared immediately. It became edematous within a few minutes and was present at the end of one week, appearing as a lichenified scaly patch. The patient has been receiving injections of histamine phosphate twice a week, for a total of eight injections. She claims that she has had no recurrence of the eruption since treatment, in spite of the fact that she has not avoided the cause.

#### DISCUSSION

DR E WILLIAM ABRAMOWITZ In most instances of physical allergy it is difficult to demonstrate passive transfer. The treatment is interesting, and I hope that the improvement continues.

DR JACK WOLF The response to treatment is most interesting and brings to mind the results obtained with histaminase in the treatment of allergic manifestations. It was found fairly useless, except in occasional cases of physical allergy.

DR GEORGE M LEWIS I wondered whether anything had been applied to the eyelid since the patient has ceased to have these attacks.

DR MAX SCHEER Did you try applying ice?

DR MAURICE J COSTELLO No, I told her not to. I once heard that histamine should be of value in treating the physical allergies, if it were to be of value at all. I do not think that there is a psychogenic factor in this case. The patient is not neurotic. Soon after the injection of histamine phosphate in very small doses, the eruption cleared. I think that there is a definite relationship between the treatment and the result. My colleagues and I are now using histamine in treatment of about 20 patients with atopic eczema, urticaria and similar eruptions, and although I have not formed any definite opinion as yet the great majority have improved some as remarkably as this patient.

### A Case for Diagnosis (Granuloma Annulare, Tuberculid?) Presented by DR ISADORE ROSEN

A D, a youth aged 20, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec 11, 1944, with an eruption on the left side of the face of eighteen months' duration, which appeared six months after he entered the army. It began with a small lesion on the left side of the face and gradually extended to involve the whole left side of the face.

The eruption consists of discrete nodules, many of which are brown and covered with scales. At the border near the nose, on the upper lip and below the ear there are elongated lesions composed of raised nodules.

An examination showed that the urine and the blood were normal. The Kahn and Wassermann reactions of the blood were negative. A tuberculin test done a few months ago at Fort Bragg, N. C., elicited a 4 plus reaction, while the one at the clinic at the Skin and Cancer Hospital elicited a negative reaction. A roentgenogram was reported from Fort Bragg as showing a normal chest. A biopsy performed a few months ago at the army hospital was reported as revealing

the pathologic conditions characteristic of lupus erythematosus At the clinic here the histologic report was lupus vulgaris

The past and family histories were essentially irrelevant

#### DISCUSSION

DR WILBERT SACHS This case belongs to the group of cases of tuberculosis. Definite tubercles and a tremendous reaction are present. I called the disease lupus vulgaris. There is no evidence of granuloma annulare. It may be one of the other types of tuberculosis falling into the class of lupus vulgaris.

DR MAX SCHEER In a case of this kind, with a clinical appearance of lupus vulgaris and a fairly extensive eruption, one would expect to find at least one or more apple-jelly nodules. I cannot offer a diagnosis, but clinically I do not think that it is lupus vulgaris.

DR WILBERT SACHS As far as apple-jelly nodules are concerned, that presupposes that one obliterates the surrounding inflammatory reaction. One may not be able to see apple-jelly nodules if the lesion is deep.

DR HERMAN SHARLIT I examined the biopsy section and saw tubercles scattered all through this lesion. I still think that while one must say that the lesion is a tuberculid I am not convinced that one is compelled to say that it is lupus vulgaris, but it is a tuberculid of some kind.

DR FRED WISE I agree with Dr Sharlit. I believe that one is dealing with tuberculosis of the skin, but the clinical picture is not that of lupus vulgaris.

DR E WILLIAM ABRAMOWITZ I had heard that the patient was under the care of Major Leifer and that a definite diagnosis of lupus erythematosus was made histologically. Nevertheless, the definite annular lesions with areas of infiltration at the edges and the short duration suggested granuloma annulare. The presence of tubercles in the biopsy specimen is disconcerting, and it still may be some unusual type of tuberculosis of the skin.

DR VAN ALSTYNE H CORNELL (by invitation) I agree with the statements made by Dr Sachs.

DR DAVID BLOOM I favor the diagnosis of tuberculid.

DR MAURICE J COSTELLO I think that the patient has some form of tuberculosis of the skin, probably a sharp allergic response to previous infection. It might almost be one-sided tuberculid of Lewandowsky. It would be interesting to perform tuberculin tests. I suggest gold therapy.

DR JACK WOLF Even if there is no agreement on the clinical diagnosis, a histologic diagnosis of tuberculosis must be accepted, and time will probably help in telling what the type is.

# Directory of Dermatologic Societies \*

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### TENTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY

Oliver S Ormsby, President, 25 E Washington St, Chicago  
Paul A O'Leary, Secretary-General, 102-2d Ave S W, Rochester, Minn  
Place New York Time Postponed indefinitely

### PAN AMERICAN MEDICAL ASSOCIATION, SECTION OF DERMATOLOGY AND SYPHILOLOGY

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President Senior dermatologist in whichever city a meeting is convened  
G A Grant Peterkin, Secretary, 4 Walker St, Edinburgh 3, Scotland

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Henry E Michelson, President, 715 Medical Arts Bldg Minneapolis  
S William Becker, Secretary, 55 E Washington St Chicago 2

\* Secretaries of dermatologic societies are requested to furnish the information  
necessary for the editor to make this list complete and to keep it up to date

## SECTIONAL

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Place Academy of Medicine of Northern New Jersey, Newark Time Third  
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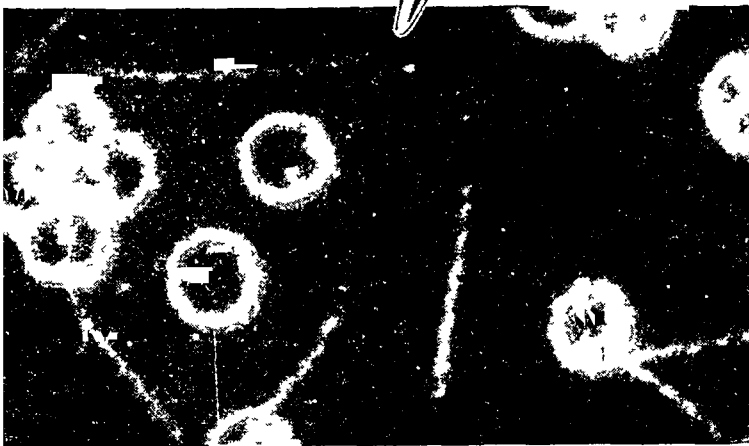
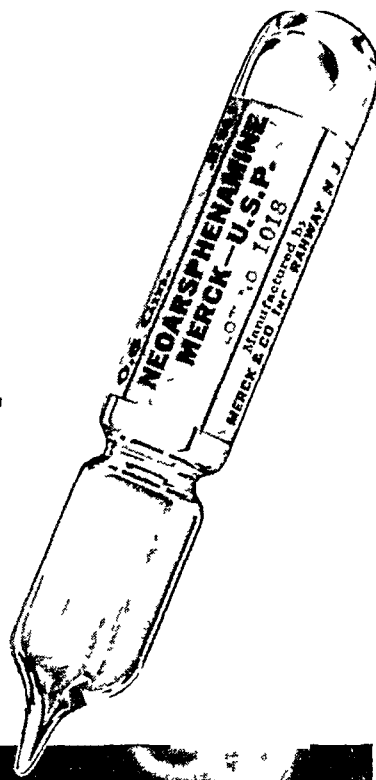
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\*Padgett, P., Long-term results in treatment of early syphilis, *J. A. M. A.* 116 7-11, 1941

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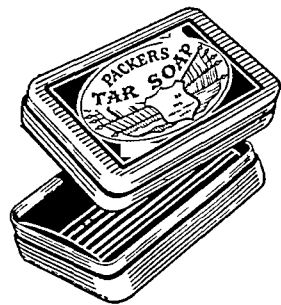


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- Penicillin in Dermatology A Study of One Hundred and Seventy Four Cases Captain Orlando Canizares Medical Corps, Army of the United States
- Preservation of Virulence of Treponema Pallidum Some Additional Laboratory Methods Ernest K Stratton, M D, San Francisco
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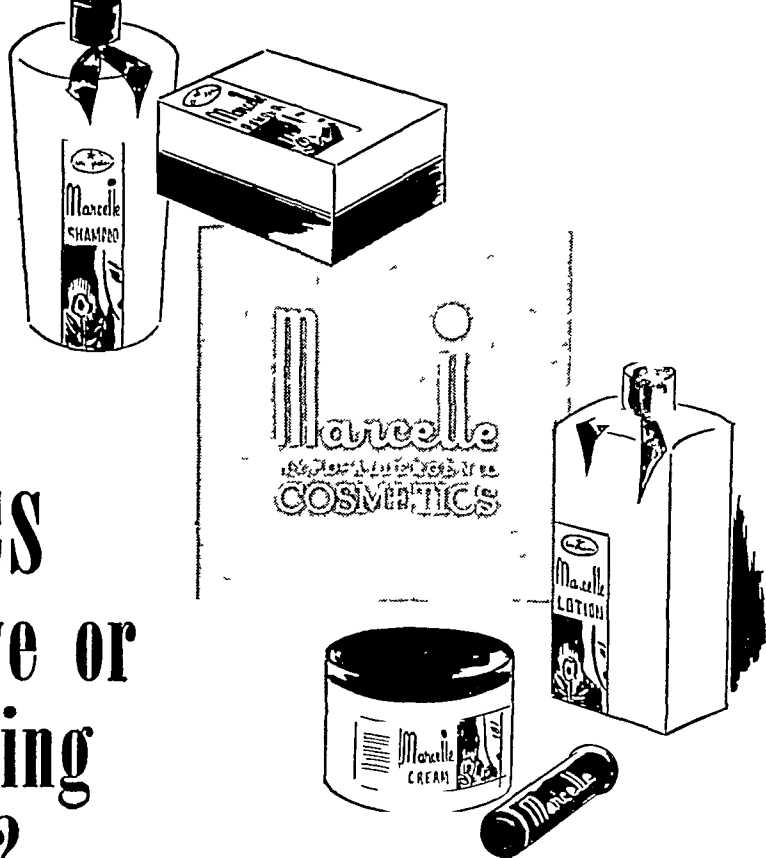
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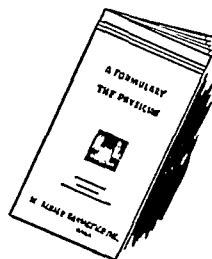


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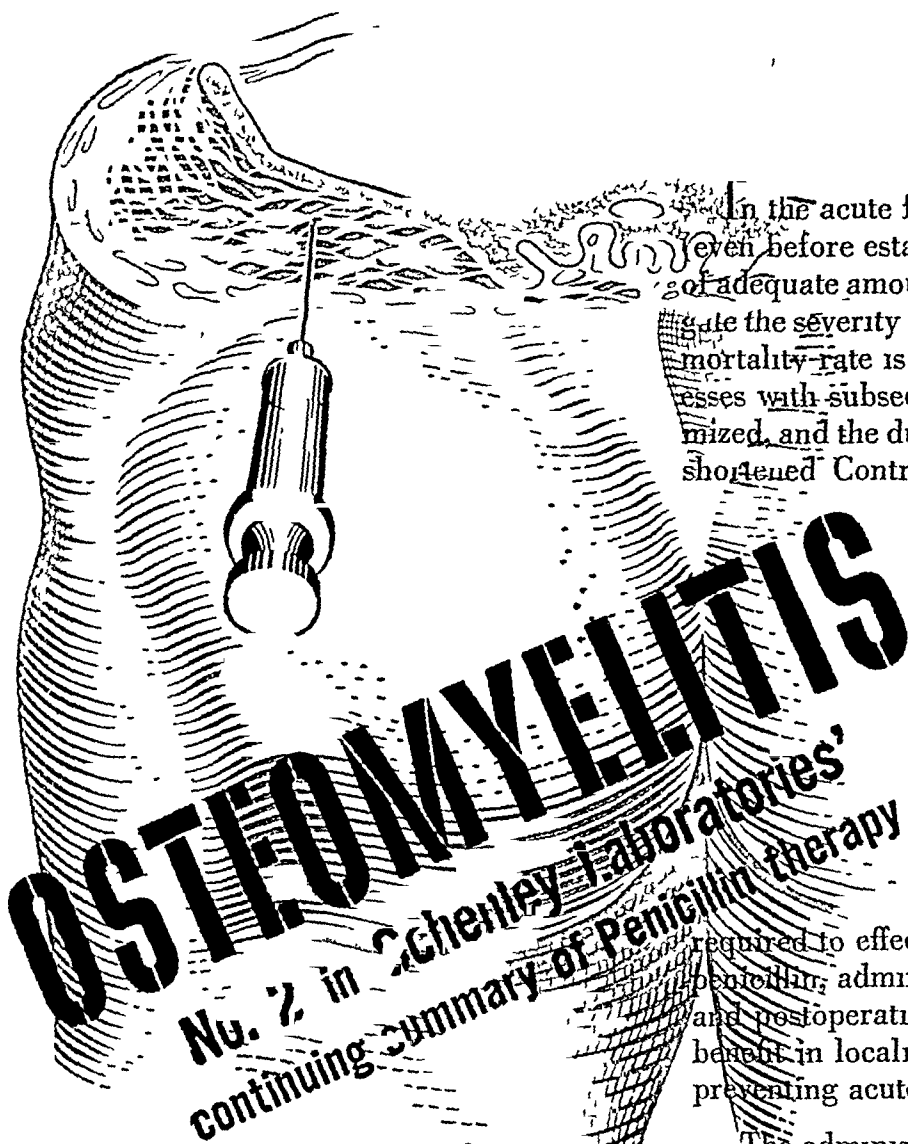
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ALTEMEIER, W. A. *Treatment of Acute Hematogenous Osteomyelitis with Penicillin*, *Ohio State M J* 42 489 (May) 1946.



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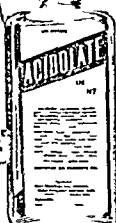
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<sup>1</sup>Swartz J. H. and Blank I. H. J. A. M. A. 125:30 (May 6) 1944

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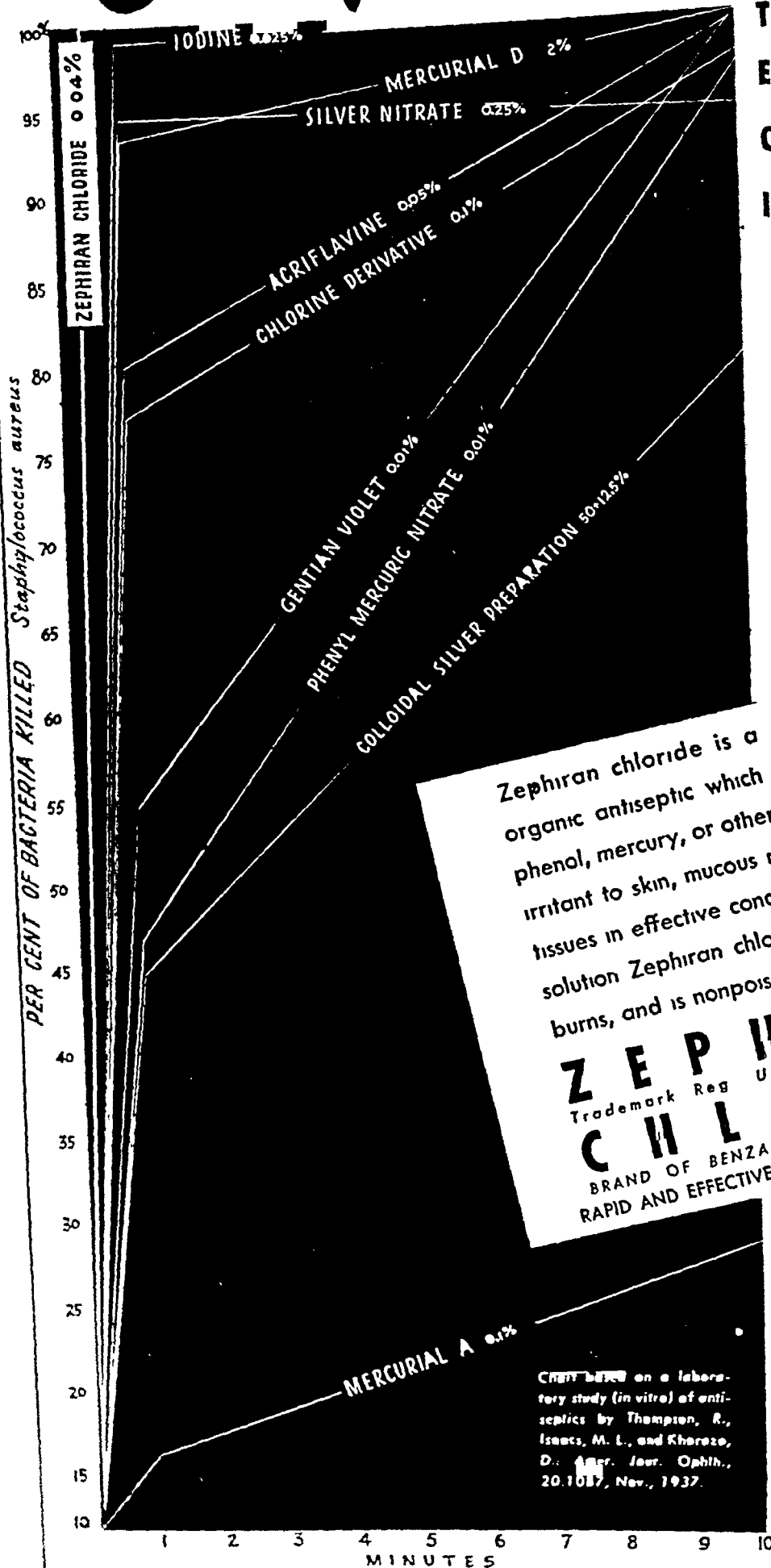
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<sup>1</sup> U.S. Nav. M. Bull. 45 783, 1945, and previous annual Navy reports.

<sup>2</sup> Stokes, J. H., Beerman, H. and Ingraham, N. R. *Modern Clinical Syphilology*, ed. 3, Philadelphia, W. B. Saunders Company, 1945, pp. 359, 300.



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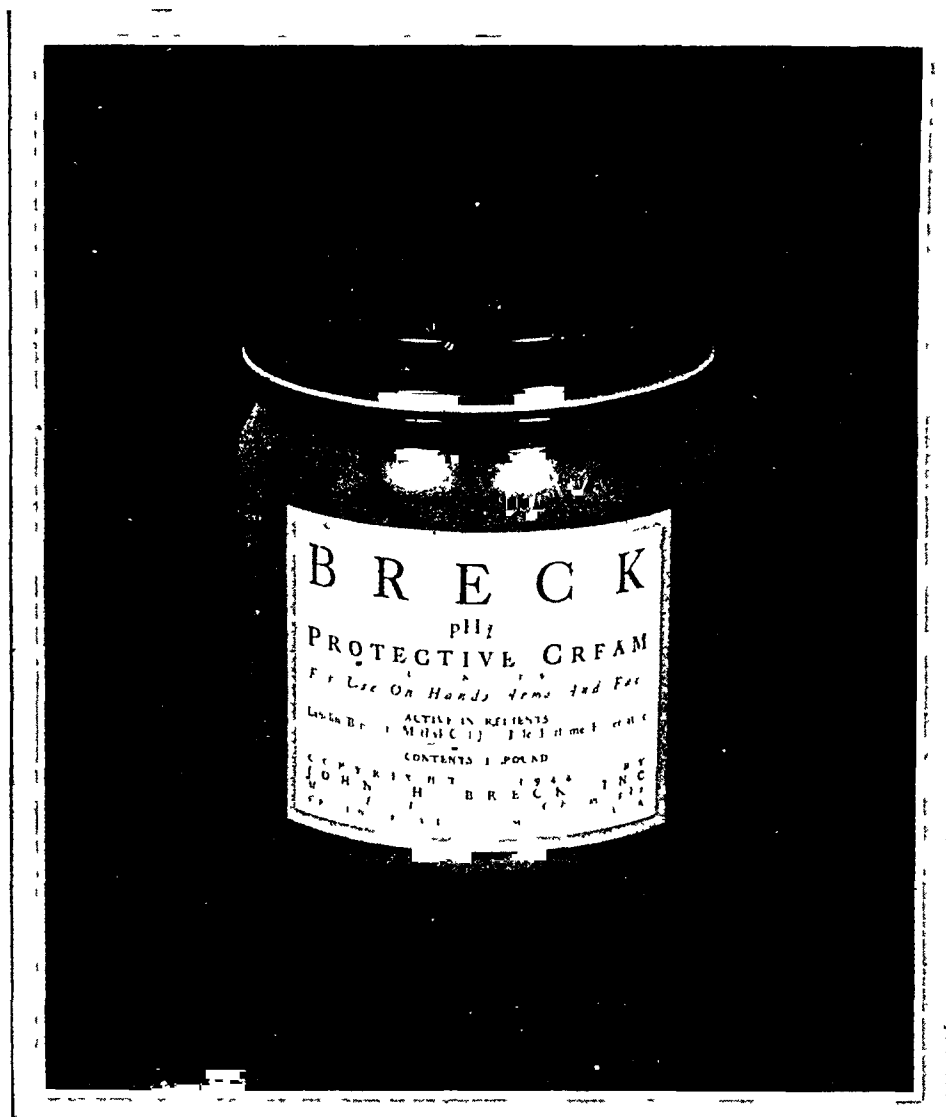
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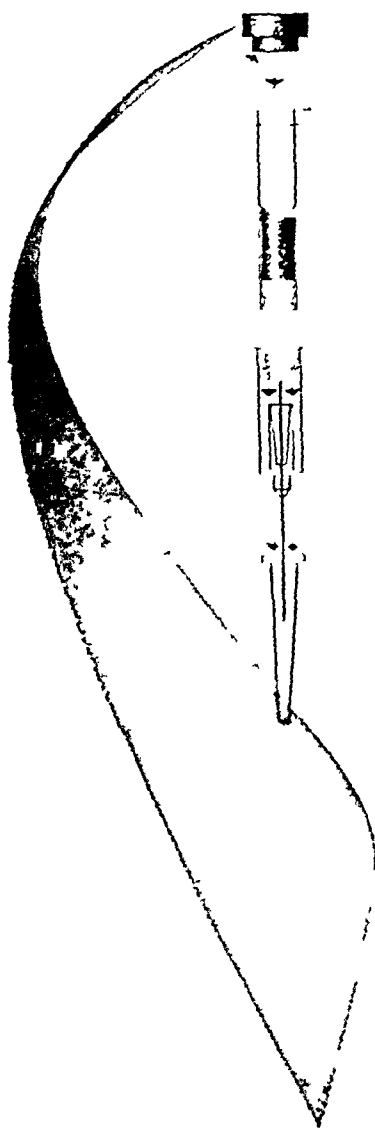


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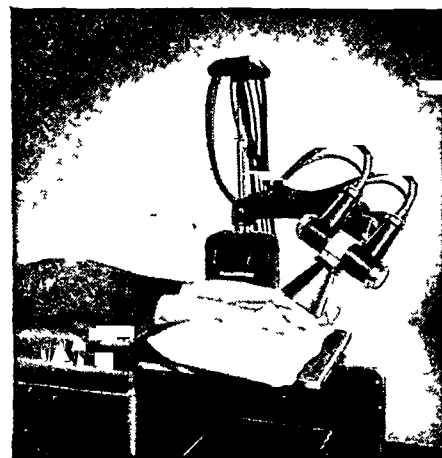
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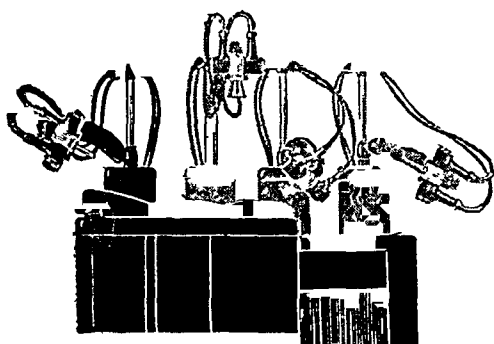
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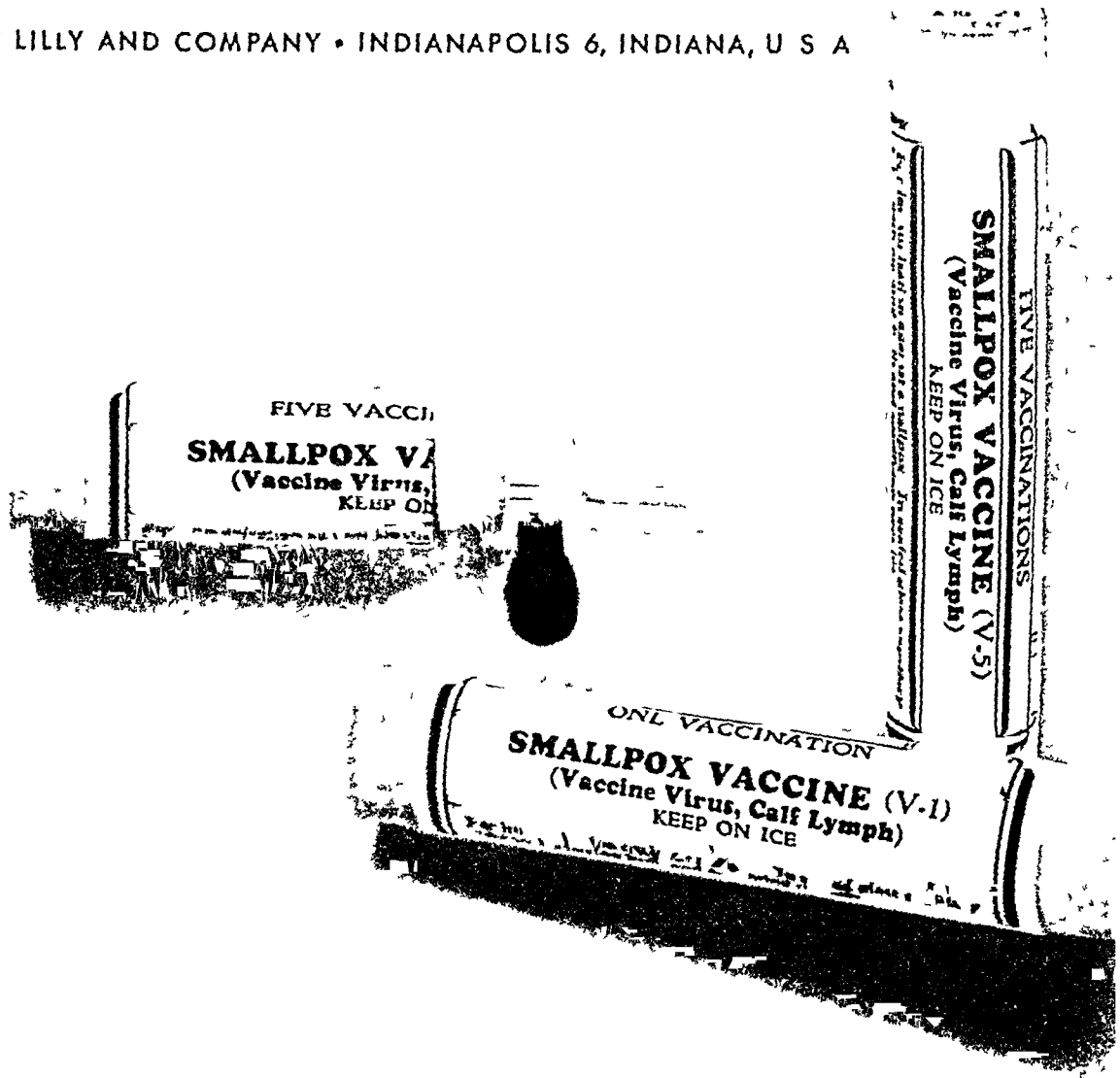


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# Archives of Dermatology and Syphilology

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## TREATMENT OF BASAL CELL EPITHELIOMA BY INJECTION OF TISSUE EXTRACTS

A Preliminary Report

JOSEPH C. AMERSBACH, M.D.

ELSIE M. WALTER, M.A.

AND

GEORGE SPERI SPERTI, Sc.D.

NEW YORK

A GREAT deal of research work has been done in an effort to find a way of treating cancer biologically by nondestructive methods, i.e., methods other than surgical intervention and irradiation. Early experimenters attempted to induce resistance in laboratory animals by inoculation with material from tumors. Ehrlich,<sup>1</sup> Lewin,<sup>2</sup> Kepinow<sup>3</sup> and Koenigsfeld<sup>4</sup> reported successful results, however, Hertwig and Poll,<sup>5</sup> Borrel,<sup>6</sup> Gierke,<sup>7</sup> Frankel and Furer<sup>8</sup> and Wood<sup>9</sup> were unable

\* This research was made possible partly through a grant from the Lillia Babbitt Hyde Foundation.

Read in part before the Section of Dermatology and Syphilology at the Ninety-Seventh Annual Meeting of the American Medical Association, San Francisco, July 3, 1946.

† From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University, as part of a collaborative research program with the Institutum Divi Thomae, Cincinnati.

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to induce any resistance in their experimental animals. Since the different investigators did not use the same method of treatment, it is difficult to compare their results and to draw definite conclusions.

Almost coincidental with the work on the immunization of animals by tumor inoculations were investigations of the immunizing power of tissues other than neoplasms. Many tissues were used, but of particular interest in this paper are spleen and liver. Levin<sup>10</sup> was able to demonstrate the development of decided resistance to tumor growth by the injection of autolyzed liver of rats naturally resistant to the tumor. Levin<sup>11</sup> also reported positive results in experiments in which normal skin and spleen tissue of a mouse were inoculated subcutaneously into rats. Higuchi<sup>12</sup> reported some positive results in experiments using placenta, blood, embryonic skin, mammary gland and spleen to induce resistance against the carcinoma of the mouse. Itami<sup>13</sup> demonstrated the power of normal embryonic liver to induce resistance to transplantable tumors. Oser and Pribram<sup>14</sup> found that the injection of spleen pulp into sarcoma-implanted rats sometimes resulted in shrinkage of the tumors and at other times brought the tumor growth to a standstill. Bungeler,<sup>15</sup> using spleen implants on the Ehrlich adenocarcinoma and on a malignant chondroma of two weeks' growth, found little if any effect on the final development of the tumor. Fichera<sup>16</sup> transplanted bits of spleen and thymus from the fetus to cancerous patients, with little success. Later he prepared extracts from these organs which were used in treating 300 patients, 100 of whom had inoperable cancer. At the end of three years regres-

10 Levin, I. Resistance to the Growth of Cancer Induced in Rats by Injection of Autolyzed Rat Tissue, *Proc Soc Exper Biol & Med* **7** 64-67, 1909

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sions had occurred in 9 per cent of the patients and the tumors had become stationary in 8 per cent

Even though there is substantial agreement on the power of some tissues to immunize or cause regression of a tumor, there has been decided disagreement as to whether or not the cells used for building resistance must be living. It seemed, however, that only living cells have this power, according to the experiments of Michaelis,<sup>17</sup> Ehrlich and Bashford (as cited by Levin<sup>18</sup>), Flexner and Jobling,<sup>19</sup> Woglom,<sup>20</sup> Haaland,<sup>21</sup> von Graff and Ranzi,<sup>22</sup> Pitzman<sup>23</sup> and Chambers and Scott.<sup>24</sup> In view of the limited or questionable success of experiments in which nonliving cells were used as the immunizing agent, it is not at all surprising that few reports of successful experiments are to be found in the literature on the use of cellular extracts as immunizing agents. Chambers and Scott<sup>24</sup> expressed the belief that the agent causing immunity to tumors in the case of the Jensen rat carcinoma was a soluble product of the dead tumor cells formed as a result of enzymatic action. Fardon,<sup>25</sup> using a strain of heterozygous market albino mice and the mammary adenocarcinoma 63, found that mice could be rendered resistant by injections of a cell-free extract of normal tissues. His results showed that the active immunizing fraction is water soluble, may be separated from the tissue pulp and need

17 Michaelis, L. Versuche zur Erzielung einer Krebsimmunität bei Mäusen, *Ztschr f Krebsforsch* 5:191-197, 1907

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not be linked to the living cell Domagk and Hackmann<sup>26</sup> also obtained satisfactory results with cell-free water extracts from tumor and from normal tissue Using the Ehrlich mouse carcinoma, the Jensen rat sarcoma and the Brown-Pearce rabbit carcinoma, they obtained distinct resistance with the cell-free fraction against subsequent tumor implantation In the case of established tumors, however, they found that large doses of the fraction stimulated the growth of the neoplasms

As late as 1936 Murphy<sup>27</sup> stated that clearcut results had not been obtained in attempts to influence susceptibility with serum and with tissue and organ extracts, but definite resistance to transplantable tumors had been obtained only in the early investigations in which living homologous normal cells were used Lewisohn<sup>28</sup> tested the effect of a water-soluble beef spleen extract on mouse sarcoma 180 Of the 281 treated sarcomas, 60 per cent were absorbed and considered as healed with no recurrence during a period of five months, while 8 per cent of the 290 controls were found to have regressed spontaneously He reported that low concentrations of the extract had great stimulatory effects on the tumors Fardon<sup>29</sup> demonstrated that the immunizing principle from spleen extracts was not a protein fraction In fact, in his experiments he demonstrated that increased susceptibility resulted from the injection of the protein fraction Bauer and others<sup>29</sup> carried out an investigation on 879 mice with transplantable Ehrlich carcinoma They concluded that the alcoholic extract of the spleen tissue had an inhibiting action on the development of tumors and that purification of the extract with benzene doubled the activity of the extract Lewisohn and others<sup>30</sup> precipitated the protein fraction from their extract and introduced their fraction intravenously rather than subcutaneously This method of administration was successful, but the effects followed a different course from those obtained by subcutaneous injections

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29 Bauer, E, Khaletzkaya, F Lwisoa, A, and Shabad, L M The Inhibition of Tumor Growth by Some Fractions of Extracts of Spleen Tissue, *Acta cancerol* **2** 17-26, 1936

30 Lewisohn, R, Leuchtenberger, R, and Laszlo, D Spleen Extract in the Treatment of Transplanted and Spontaneous Malignant Tumors in Mice, *Surg, Gynec & Obst* **71** 274-285, 1940

In connection with the work on immunity and regression of tumors, the metabolism of cancerous tissue is of interest. Warburg,<sup>31</sup> in his epoch-making researches, reported that the respiration of carcinoma tissue was less than that of kidney and liver. In spite of the breakdown of some of Warburg's original claims, Burk<sup>32</sup> has upheld the contention that malignant tissues differ from normal ones in their metabolism. He pointed out that the sum of many metabolic characteristics must be taken into consideration for full differentiation between normal and malignant tissues. Amersbach, Walter and Cook<sup>33</sup> found alterations in the respiration of precancerous lesions and epitheliomas from that of the normal epithelium of the same general area. Davis<sup>34</sup> and Bungeler<sup>35</sup> found that the respiration of normal tissues of a strain of mice which is resistant to a transplantable tumor is considerably higher than the average respiration of the normal tissues of a susceptible strain. Bungeler demonstrated the power of a fairly crude spleen extract to stimulate the respiration and depress the glycolysis of tumors. Sperti<sup>36</sup> described the respiration-stimulating power of a beef spleen extract on a mouse sarcoma. Fardon, Brotzge and Loeffler<sup>37</sup> observed that "an injection of placental suspension (immunizing agent) into mice definitely stimulates the oxygen consumption of the skin." Schroeder and Cook<sup>38</sup> found that extracts

31 Warburg, O. The Metabolism of Carcinoma Cells, *J. Cancer Research* 9 148-164, 1925

32 Burk, D., in Ward, H. B. Some Fundamental Aspects of the Cancer Problem, New York, The Science Press, 1937, p. 121, On the Specificity of Glycolysis in Malignant Tumors as Compared with Homologous Adult or Growing Liver Tissues, in A Symposium on Respiratory Enzymes, Madison, University of Wisconsin Press, 1942, pp. 235-245. Burk, D., Sprince, H., Spangler, J. M., Kabat, E. A., Furth, J., and Claude, A. The Metabolism of Chicken Tumors, *J. Nat. Cancer Inst.* 2 201-240, 1941.

33 Amersbach, J. C., Walter, E. M., and Cook, E. S. Respiration of Human Keratoses and Epitheliomas, *Arch. Dermat. & Syph.* 46 269-275 (Aug.) 1942.

34 Davis, J. E. Biochemical Differences Between Mice of Tumour and Non-Tumour Strain, and Tumour-and Non-Tumour-Bearing Mice of Tumour Strain, *Canad. M. A. J.* 36 27-30, 1937.

35 Bungeler, W. Tierexperimentelle und zellphysiologische Untersuchungen zur Frage der allgemeinen Geschwulstdisposition, *Frankfurt Ztschr. f. Path.* 39 314-402, 1930.

36 Sperti, G. S. Radiations, Cellular Metabolism and Cancer Resistance, *Stud. Inst. Divi. Thomae* 3 17-38, 1941.

37 Fardon, J. C., Brotzge, G. C., and Loeffler, Sister M. K. The Relation of Induced Tumor Resistance to Increased Tissue Respiration, *Stud. Inst. Divi. Thomae* 3 61-68, 1941.

38 Schroeder, Sister M. P., and Cook, E. S. The Effects of Tissue Extracts on the Respiration and Glycolysis of Some Normal and Tumor Tissues, *Stud. Inst. Divi. Thomae* 2 247-258, 1939.



from yeast and normal tissues increase respiration and depress both the aerobic and anaerobic glycolysis of normal liver and tumor tissues

There seems to be evidence to indicate that agents which have the power to build resistance to tumor growth may have the power to affect the metabolism of malignant tissues. However it has not been demonstrated that all substances which have the power to stimulate respiration likewise have the power to induce the resistant state.

The interrelation between respiration and glycolysis, and immunity to tumors, is discussed at some length by Spert<sup>36</sup> in a review on cellular metabolism and resistance to cancer.

Since it had been shown that spleen and liver extracts gave good results in the experiments on animals and the extracts seemed to have a beneficial result on the metabolism of cancerous tissue, it was decided to test their effect in the treatment of human epitheliomas. Tumors of low malignancy, which were localized and easily accessible, were used to make certain that any effectiveness of the fraction could be readily observed. Basal cell epitheliomas seemed to offer the best type of neoplasm for the investigations.

#### THE PREPARATION OF SPLEEN AND LIVER EXTRACTS

Normal human spleens and livers were collected at autopsy. In all cases care was taken not to use tissues from cadavers which had been standing more than twenty-four hours. Only those of persons who had died suddenly, as a result of accident or heart disease, were used.

The liver and spleen extracts were prepared separately. The tissues were weighed, trimmed of all fat and extraneous connective tissue and ground thoroughly and added to a volume of distilled water corresponding to the weight of the tissue, i e, 100 cc of water per hundred gram of spleen. The suspension was frozen and thawed three times, allowing one day for each freezing and thawing procedure. The proteins were then precipitated by adding increasing concentrations of 95 per cent alcohol to the mixture. First, alcohol was added to a final concentration of 50 per cent, and the mixture was allowed to stand for two hours. Finally, the concentration was raised to 80 per cent, the mixture allowed to stand for one day and filtered free of tissue and precipitated protein. The extract was concentrated approximately to the volume of distilled water added originally. This water solution was then extracted with three separate portions of ether of a total volume equal to that of the water solution. The ether solution was discarded, and the water solution was evaporated almost to dryness. The residue was made up to the desired concentration with distilled water.

In the earlier work a concentration of 1 cc, equivalent to 1 Gm of tissue, was used, that is, the volume of the final solution was the same in cubic centimeters as the weight in grams of the tissue extracted. In the later work a concentration of 1 cc, equivalent to 9 Gm, was used, that is, a volume equal to one ninth of the weight of the tissue in grams. The  $p_H$  of the extract was adjusted to 6.5 to 7 with potassium hydroxide, and the extract was boiled for thirty minutes. After standing in the refrigerator overnight, the solution was filtered. The extract was then put into serum bottles and boiled for thirty minutes on each of three successive days. Each sample of extract prepared was

tested for toxicity by injecting into a guinea pig the same amount to be used subsequently on the patients. In no case were any ill effects shown by the animals or the patients.

#### CLINICAL PROCEDURE

At the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, patients were selected with small basal cell epitheliomas varying in size from that of a pea to 3 or 4 cm in the longest dimension. All types of basal cell epitheliomas were taken indiscriminately as they appeared in the clinic service. Before any treatment was given, a colored photograph was taken of the lesion and a biopsy was also performed for pathologic diagnosis of the lesion. The patient was then given a series of weekly injections of either spleen or liver extract and observed closely. The patient occasionally missed an injection, or occasionally it was deemed advisable to allow a longer time to elapse between the injections, as for example, when a crust was present.

Injections were made intradermally, for it has been shown repeatedly by Besredka and Gross<sup>39</sup> that the intradermal route was successful; they produced immunity to tumors in animals by the intradermal injection of tumor suspension. Cheever and Janeway<sup>40</sup> also used the intradermal method in successfully inducing resistance against the Brown-Pearce carcinoma. Generally 1 cc of extract was injected, although when the location was such or the lesion had regressed until it was very small only 0.25 cc or 0.5 cc was used. Occasionally if the lesion was large 1.5 cc or 2 cc of extract was necessary to infiltrate it well. At each treatment the lesion was infiltrated until it and the surrounding tissue for about  $\frac{1}{4}$  inch (0.6 cm) became blanched and hard.

In some cases, especially with the liver extract, the patients found the injections painful and a small amount (0.25 to 1 cc) of 2 per cent solution of epinephrine-free procaine hydrochloride was given a few minutes preceding the injection. Some patients received no procaine, and others did not receive it at all injections. Procaine did not seem to influence the course of the regression of the lesion.

It was thought that the regression of the epitheliomas to the extract might be nonspecific and was due simply to a sclerosing action of the material. It was therefore decided to treat several patients with a dextrose solution of a concentration equal to that of the spleen extract, which was 275 mg per cubic centimeter. Dextrose was employed because it is successfully used in the clinic for sclerosing varicose veins. Four patients were given the control dextrose solution at weekly intervals and observed carefully. Each received from five to seven injections, which number had been more than sufficient to elicit a response with the extracts. When all lesions failed to respond, photographs were taken and the patients were given liver or spleen extract.

A further check was made on the specificity of the extracts by testing them on normal skin. Intradermal injections of the dextrose solution and the liver

<sup>39</sup> Besredka, A., and Gross, L. Du rôle de la peau dans la sarcomatose de la souris. *Ann Inst Pasteur* 55: 402-416, 1935. De l'immunisation contre le sarcome de la souris par la voie intracutane. *ibid* 55: 491-500, 1935. Gross, L. Experimental Immunization Against Implantation of Cancer. *Quart Bull Polish Inst Arts & Sc America* 1: 418-430, 1943.

<sup>40</sup> Cheever, F. S., and Janeway, C. A. Immunity Induced Against the Brown-Pearce Carcinoma. *Cancer Research* 1: 23-27, 1941.

*Case Histories of Patients Treated with Tissue Extracts*

Case	Sex	Age	Location and Description of Lesion	Pathologic Report	Treatment	Duration of Treatment	Result
Preliminary R W	M	41	Pea sized lesion with rolled pearly borders and central ulceration on right side of nose	Basal cell epithelioma	Spleen, 7 injections 1 cc = 1 Gm, 8 injections, 1 cc = 3 Gm, 1 cc each injection	3/25/42 to 5/6/42	Definite regression but patient failed to continue treatment
Preliminary I R	F	55	Pea sized lesion with typical rolled pearly borders on center of forehead	Basal cell epithelioma	Spleen, 7 injections, 1 cc = 6 Gm, 1 cc each injection	7/27/42 to 10/2/42	Definite regression but patient failed to continue treatment
1 E Y	F	61	Pea sized raised lesion on preauricular region	Basal cell epithelioma	Spleen 8 injections, 1 cc = 6 Gm, 16 injections, 1 cc = 9 Gm, 1 cc each injection	1/20/43 to 7/28/43	Complete regression
2 J M	M	60	Dime sized raised ulcerated lesion with pearly borders on left temple	Basal cell epithelioma	Spleen, 10 injection, 1 cc = 6 Gm, 3 injections, 1 cc = 8 Gm, 2 injections, 1 cc = 9 Gm, 1 cc each injection	1/25/43 to 5/3/43	Complete regression
3 I W	M	81	Dime sized red lesion with slightly raised borders on back of right hand	Senile keratosis	Spleen, 10 injections, 1 cc = 9 Gm, 1 cc each injection	6/7/43 to 10/27/43	Complete regression
4 J M	F	75	Large pea sized lesion with rolled waxy borders on forehead	Basal cell epithelioma	Spleen, 2 injections, 1 cc = 8 Gm, 6 injections, 1 cc = 9 Gm, 1 cc each injection	5/24/43 to 8/6/43	Complete regression
5 M K	F	71	Large raised pearly pea sized lesion on right side of nose	Basal cell epithelioma	Spleen, 6 injections, 1 cc = 9 Gm, 1 cc each injection	6/30/43 to 8/4/43	Complete regression
6 T G	M	71	Pea sized raised pearly lesion just under left eyelid	Basal cell epithelioma	Spleen, 20 injections, 1 cc = 9 Gm, 2 injections, 1 cc = 15 Gm, 1 cc each injection	7/21/43 to 5/31/44	Failed to regress
7 M P	M	33	Pea sized elevated lesion with pearly wall and crust formation on right nasolabial fold	Basal cell epithelioma	Dextrose, 7 injections, 275 mg /cc Spleen, 7 injections, 1 cc = 9 Gm	8/16/43 to 10/20/43 10/27/43 to 2/9/44	No apparent response to dextrose Complete regression
8 B A	M	83	Large lesion, 3 by 1.5 cm, with rolled pearly edges and central ulceration	Basal cell epithelioma	Dextrose, 0 injections, 275 mg/cc Spleen, 17 injections, 1 cc = 9 Gm, 1 cc each injection, 8 injections, 1 cc = 15 Gm, 0.5 cc each injection	9/15/43 to 10/13/43 10/27/43 to 9/20/44	No apparent response to dextrose Still under treatment, approximately 80% regression
9 E P	F	51	Finger nail sized area, studded with waxy hard transparent nodules on left cheek	Basal cell epithelioma	Dextrose, 5 injections, 275 mg /cc Liver, 18 injections, 1 cc = 9 Gm, 6 injections, 1 cc = 15 Gm, 1 cc each injection	9/15/43 to 10/20/43 11/3/43 to 10/30/44	No apparent response to dextrose Still under treatment, approximately 75% regression

10	A R	F	63	Large pearly crusted lesion with rolled border on left preauricular region	Spino basal cell epithelioma	Liver, 10 injections, 1 cc = 9 Gm. Liver, 1 injection, 1 cc = 15 Gm. 0.5 cc each injection	10/6/43 to 6/5/44	Complete regression
11	D R	M	67	Pear sized infiltrated ulcerated lesion on right ear	Basal cell epithelioma	Dextrose, 6 injections, 275 mg /cc	10/14/43 to 11/9/43	No apparent response to dextrose
12	M M	M	64	Dime sized ulcerated lesion with pearly borders on right cheek	Basal cell epithelioma	Spleen, 3 injections, 1 cc = 9 Gm, 1 cc each injection	12/13/43 to 1/5/44	Complete regression
13	C S	M	57	Dime sized lesion with slightly rolled borders on forehead	Basal cell epithelioma	Liver, 15 injections, 1 cc = 9 Gm, 1 cc each injection, 3 injections, 1 cc = 15 Gm, 0.5 cc each injection	10/1/43 to 7/12/44	Still under treatment, approximately 90% regression
14	C S	M	70	Dime sized raised crusted lesion on right breast	Basal cell epithelioma	Liver, 4 injections, 1 cc = 9 Gm, 1 cc each injection, 9 injections, 0.25 cc	10/13/43 to 7/28/44	Complete regression
15	M H	F	70	Dime sized ulcerated lesion with pearly borders on left cheek near eye	Basal cell epithelioma	Spleen, 19 injections, 1 cc = 9 Gm, 1 cc each injection	10/25/43 to 5/8/44	Approximately 50% regression, patient failed to return for treatment
16	I S	M	53	Large, pea sized, infiltrated lesion with pearly borders and central ulceration on left temple	Basal cell epithelioma	Liver, 21 injections, 1 cc = 9 Gm, 1 cc each injection, 3 injections, 1 cc = 15 Gm, 0.5 cc each injection	10/27/43 to 7/5/44	Complete regression
17	W M	M	68	Dime sized pigmented lesion on left preauricular region	Basal cell epithelioma	Liver, 8 injections, 1 cc = 9 Gm, 1 cc each injection	11/1/43 to 12/20/43	Complete regression
18	R W	M	75	Half dollar sized brown smooth pearly lesion on back of neck	Seborrheic verruca with intraepidermic basal cell epithelioma	Spleen, 6 injections, 1 cc = 9 Gm 1 cc each injection	11/15/43 to 12/20/43	Complete regression
19	F G	F	49	Pea sized, slightly elevated, pigmented lesion with central depression on lateral border of left side of nose	Basal cell epithelioma	Spleen, 1 injections, 1 cc each injection, 3 injections, 1.5 cc each injection, 7 injections, 2 cc each injection, 1 cc = 9 Gm, 5 injections, 1.5 cc each injection, 5 injections, 1 cc each injection, 1 cc = 13 Gm	12/15/43 to 11/8/44	Still under treatment, 80% regression
20	M D	F	70	Dime sized eroded lesion with pearly border on right preauricular region	Basal cell epithelioma	Spleen, 15 injections, 1 cc = 9 Gm, 0.5 cc each injection, 12 injections, 1 cc = 12 Gm, 0.25 cc each injection	12/20/43 to 10/4/44	Still under treatment, approximately 30% regression
21	M L	F	33	Pea sized raised pearly lesion on center of forehead	Basal cell epithelioma	Spleen, 6 injections, 1 cc = 9 Gm, 1 cc each injection	1/3/43 to 4/24/44	Complete regression
22						Liver, 9 injections, 1 cc = 9 Gm, 0.5 cc each injection	2/23/44 to 4/12/44	Complete regression

and spleen extracts were made into the normal skin on the upper part of the arms and the thighs, 2 or 3 patients being used for each solution. In each patient the inflammation and swelling characteristic of the intradermal injection of a nonisotonic solution were noted. With the liver extract a small dark discolored area was produced, which became bullous and later produced a thin crust. This may have been an effect of the concentration. However, since the spleen extract never produced such an area and also was active in causing the regression of the basal cell epitheliomas, it seems likely that the active factor is probably nontoxic to normal skin.

The case histories are given in the table, and photographic histories of several of the cases are shown.

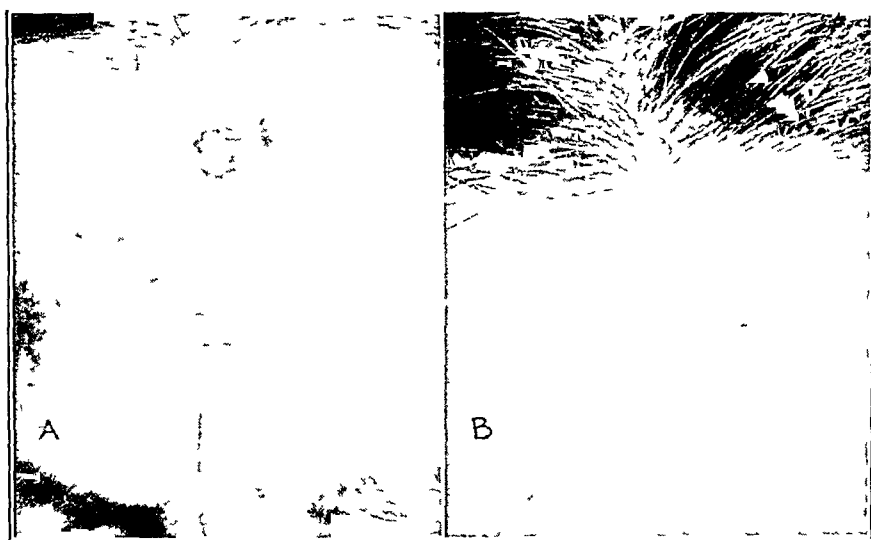


Fig 1 (case 4) —*A*, before treatment, *B*, after treatment with eight injections of spleen extract

#### COMMENT

In these experiments, 21 patients with basal cell epitheliomas were treated with extracts of liver or spleen. One patient (case 6) receiving the spleen extract failed to respond to the treatment. Of the other 20 patients, 14 continued the treatment to complete regression of the lesion as observed clinically and as shown by final biopsy of the lesion. The other 6 patients are still under treatment, but all have shown definite regression of the lesion. In some of the finished cases the cosmetic result is indeed excellent, for no scar is visible, in others, there is a scar similar to that resulting from excision, probably dependent on the amount of ulceration originally present. Four of the patients were first used as controls and given injections of a dextrose solution. All failed to respond to the injections of dextrose and were subsequently transferred to spleen or liver extract, where-

upon the lesions began to regress. In 2 cases (cases 7 and 11) the regression was rapid and required seven and three injections respectively. Lesions in the other 2 cases have been much slower to regress and have required a relatively large number of injections.

Of the 21 patients, 7 received liver extract and 14 spleen extract. It is difficult to say whether or not the spleen extract is more effective than the liver extract, for the size, type and location of the lesion and the general physical status of the patient varied greatly. In general, it appeared that the spleen extract produced a faster reaction than the liver extract.

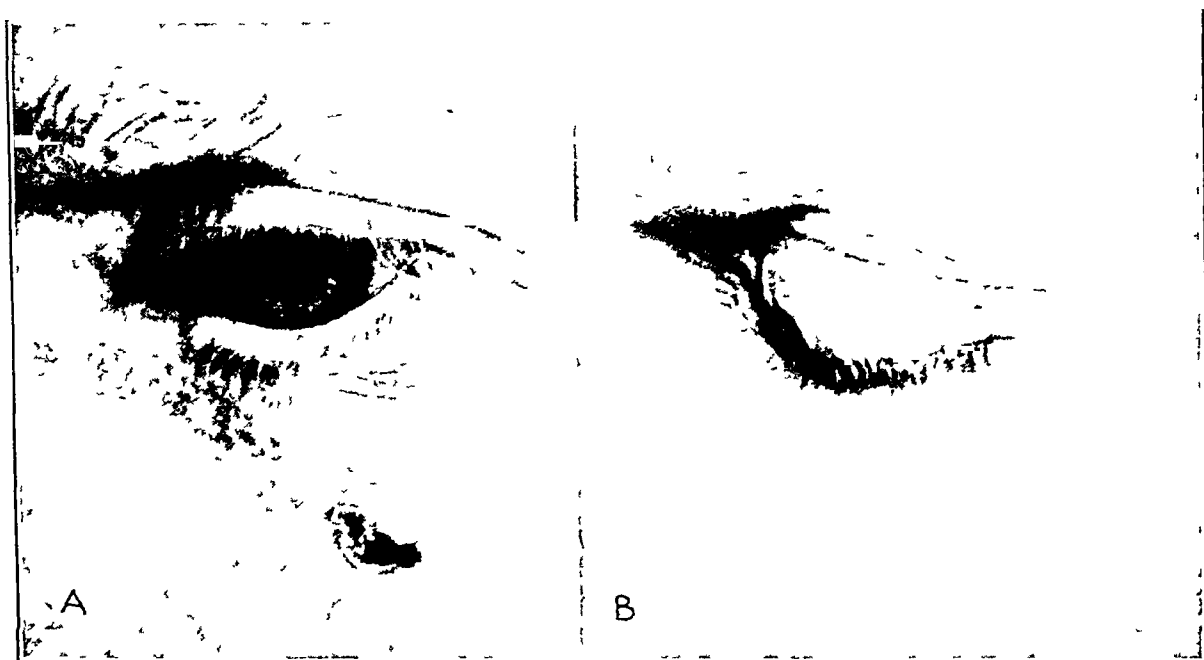


Fig 2 (case 15) —*A*, before treatment, *B*, after treatment with twenty-four injections of liver extract.

The number of injections required to cause complete regression varied a great deal according to the lesion. One patient required only three injections, several only six injections and some as many as twenty. It was noticed that in areas easily infiltrated with 1 cc of extract the lesion responded much faster than in those around the eyes and on the nose. In the latter areas generally a smaller quantity of extract was used per injection, but the response was much slower even when the total quantity of extract used was the same as that employed in treating lesions which received a larger dosage per injection. It seems that a definite minimum dose per injection is required. Also, patients who were more regular in their treatments generally responded faster.

It is likely that the composition of the extracts varied, for several different preparations were used during the course of treatment, and,

although the same method of preparation was rigidly followed and only healthy tissue was used, there were probably individual variations in the tissue employed for the preparation of successive extracts. In the early part of the work the spleens and livers were often from



Fig 3 (case 17) —*A*, before treatment, *B*, after treatment with six injections of spleen extract



Fig 4 (case 20) —*A*, before treatment, *B*, after treatment with six injections of spleen extract

young cadavers, but recently the tissue has been almost wholly from middle-aged and older persons. The effect of the variations in the source of tissue used is not known and should be investigated.

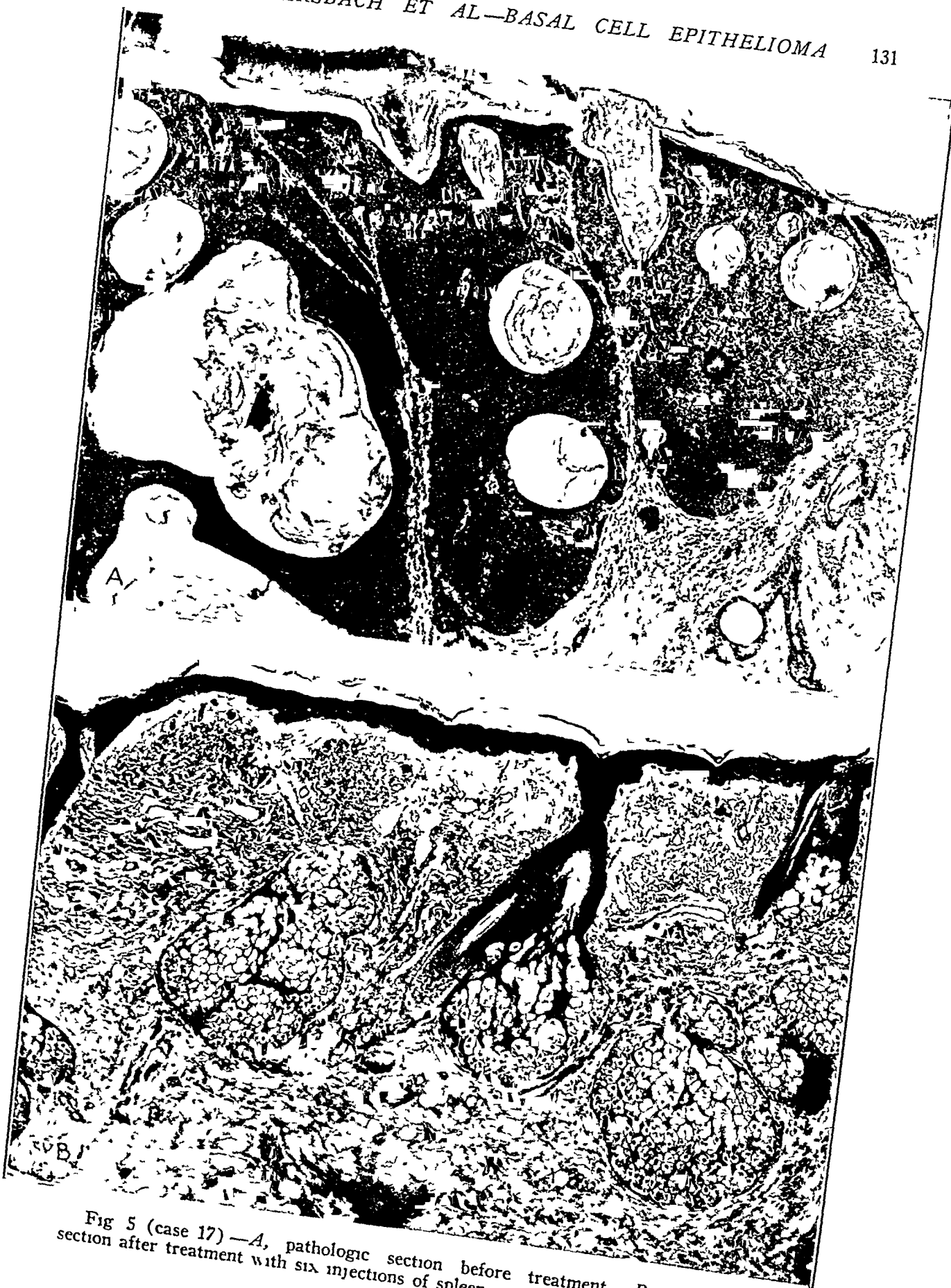


Fig 5 (case 17) — *A*, pathologic section before treatment, *B*, pathologic section after treatment with six injections of spleen extract



The lesion usually responded noticeably after the third or fourth injection, when there was a definite shrinking. In several cases the lesion appeared to regress by 50 per cent during one week between injections. A crust was generally present at some time during the regression of a lesion, in some cases the crust was thin and was replaced a number of times until the healthy tissue was finally revealed. In other cases the crust produced was dense and adhered firmly to the lesion for a number of weeks.

The extract seemed to have no effect on normal tissue, for only the lesion was affected, although the surrounding normal tissue was infiltrated at each injection. In the case that failed there was no noticeable change in lesion or surrounding tissue. Injections of spleen and liver extract into normal skin resulted in no toxic effect with the spleen extract but a slight reaction with the liver extract. Since both extracts were active in producing regressions of the epitheliomas, it seems that the active factor is probably not toxic to normal tissues.

In none of the cases observed since completion of the treatment has there been any signs of recurrence in the period of one to two years. However, it is too early to make any definite statement regarding recurrences, and the patients will be examined regularly over a period of at least five years.

#### SUMMARY

Twenty-one patients with basal cell epithelioma were treated by the injection of spleen or liver extract. The lesion of 1 treated with spleen extract failed to regress. Fourteen have had complete regression and disappearance of the lesion. The remaining 6 are still under treatment, but all have shown regression.

Dr John B Lauricella made it possible to obtain the tissue for preparation of the extract, and Dr Wilbur Sachs made the pathologic diagnosis of the lesions.

## SCLERODERMA OF THE FACE INVOLVING THE GINGIVA

Report of a Case

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AND

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WHILE cases of scleroderma are frequently encountered in clinic and private dermatologic practice, there seems to be little mention of oral involvement in the literature or in society transactions Barber<sup>1</sup> in January 1944 described a man aged 43 with a sclerodermatous lesion confined to the mucous surface of the lower lip, extending from the vermillion border to the alveolar sulcus. He also cited a report by W Anderson, in 1898, of a case of scleroderma involving the skin and mucous membranes supplied by all three divisions of the fifth cranial nerve. Looby and Burket<sup>2</sup> in 1942 reported a case of scleroderma of the face with involvement of the alveolar process. Their patient was an 8 year old girl on whose face there suddenly developed an indurated area roughly outlining the terminal distribution of the sensory divisions of the fifth nerve. She showed "deep scarring of the gingival tissue and depression of the alveolar process which, in the region of the left maxillary incisor, extended from the ridge toward the muco-buccal fold." Their paper gives an account of the historical development of the disease as well as an excellent review of the histologic features and etiologic possibilities. In 1933 a case of involvement of the skin and the buccal mucosa in a 57 year old woman was presented by Gougerot and Elhascheff<sup>3</sup> before a French dermatologic society. O'Leary and Nomland<sup>4</sup> in an extensive clinical study of 103 cases of scleroderma (55 of which were of the circumscribed type) did not mention mucosal involvement in any of them. This strengthens our conviction that circumscribed scleroderma involving the oral cavity is of sufficient rarity to warrant reporting.

1 Barber, H W. Circumscribed Scleroderma of Buccal Mucous Membrane, *Proc Roy Soc Med* **37** 73 (Jan) 1944

2 Looby, J P, and Burket, L W. Scleroderma of Face with Involvement of Alveolar Process, *Am J Orthodontics* **28** 493-498 (Sept) 1942

3 Gougerot and Elhascheff, O. Scleroderma of Buccal Mucosa and Skin, *Bull Soc franç de dermat et syph* **40** 111-112 (Jan) 1933

4 O'Leary, P A, and Nomland, R. Clinical Study of 103 Cases, *Am J. M Sc* **180** 95-112 (July) 1930

## REPORT OF A CASE

E. D., a 20 year old white woman, was seen in March 1945, she had first noticed whitish depigmentation of the tip of her nose, of the cleft of her upper lip and of a vertical midline area on her forehead in December 1944. The general examination and past history were noncontributory. The area became progressively whiter, with a faint violaceous halo at the border. On the buccal surface of her upper lip was a vertical area lighter in color than the surrounding mucosa, this extended on the gingival margin to the right upper incisor, at which point the adjacent gingiva appeared necrotic.

Biopsy of a specimen from the mucosa under the upper lip showed a broad area in the submucosa of nearly acellular and very dense collagen in which the outlines of the fibrils were indistinct. A pathologic diagnosis of scleroderma of the labial mucosa was made (Dr. Warren C. Hunter).



Scleroderma involving the gingiva

## COMMENT

In the differential diagnosis of this case, vitiligo was strongly considered (at the first examination only the alabaster-like color of the skin was noted—induration was never a conspicuous feature). This diagnosis did not explain the lesion of the gingiva, a type of lesion which neither of us had observed before. Two dentists to whom the patient was shown expressed the opinion that the gum showed an "advanced degree of pyorrhea," although they could not explain its localization about a single tooth. Histologic examination of the gingival tissue established the diagnosis of scleroderma beyond reasonable doubt.

SUMMARY

A case of circumscribed scleroderma of the face involving the gingiva is described. Judging from available reports, such cases are comparatively uncommon.

Dr. L. S. Selling permitted us to study and report this case.

Medical-Dental Building

Medical Arts Building

## USES AND ABUSES OF PENICILLIN IN DERMATOLOGY

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THE RECENT widespread employment of penicillin in the treatment of infectious dermatoses makes desirable a summary of the indications for and the contraindications to its use, as well as an analysis of the results to be expected from various methods of administration.

As reported in a previous communication,<sup>1</sup> penicillin in a water-soluble ointment base was used in the treatment of 40 patients with treatment-resistant cutaneous infections. None of the patients had previously received penicillin therapy. Cure was obtained in 66.6 per cent of patients with uncomplicated pyoderma, with the individual manifestations responding as follows: impetigo 85.7 per cent, pustular folliculitis 66.6 per cent, sycosis 60 per cent and infectious eczematoid dermatitis 55.5 per cent. Tests for sensitivity to penicillin were made on most of the patients. The trench plate method was used. In this procedure a trench was made across a blood agar plate by removing a strip 1 cm. in width. This trench was filled with agar containing 2 units of penicillin per cubic centimeter. The organism to be tested and the Florey strain of *Staphylococcus aureus* were then streaked across the trench. Sensitivity of the organisms to penicillin was shown by inhibition of growth comparable to that seen with the control.

It was found that when the causative organisms remained consistently sensitive to penicillin clinical involution of the lesions was constant, regardless of the type of cutaneous infection present. Resistance to penicillin as determined by this method, was found initially in 22.5 per cent of the cases. Follow-up tests of sensitivity to penicillin tests on patients with only temporary improvement or with relapsing lesions disclosed that an additional 15 per cent of infections had become resistant to penicillin. This phenomenon was thought to be due to the use of an inadequate concentration of penicillin, the strength of the ointment being 200 units of the drug per gram of ointment base.

This paper was prepared while the authors were in service with the Army of the United States.

<sup>1</sup> Cormia, F. E., and Maschmeyer, R. H. Therapy of Treatment-Resistant Pyoderma with Penicillin, *M. Bull. Europ. Theat. Op.*, 1944, no. 23, p. 1.

The amount of penicillin was accordingly increased to 500 units per gram of base, and further resistance to penicillin did not develop

Many questions, however, remained unanswered. Could optimum results be obtained from topical applications alone or from the simultaneous use of intramuscular injections? The results of the combined or alternate use of penicillin and the sulfonamide compounds were another matter for conjecture. Furthermore, would increasing local concentrations of penicillin be of value in treatment of infections in which the organisms manifested an increased resistance to penicillin? Lastly, the question of the use of penicillin empirically in treatment of severe infections, i. e. without a preliminary determination of sensitivity to penicillin, was opened to careful scrutiny

#### MATERIALS AND METHODS

A group of 75 patients with treatment-resistant pyoderma was selected for study. The types of pyoderma investigated included impetigo, ecthyma, pustular folliculitis, sycosis, infectious eczematoid dermatitis, furunculosis, infected sebaceous cysts and secondarily infected acne vulgaris. The etiologic agent, with but few exceptions, was a pigmented coagulase-positive hemolytic *Staph aureus*. Hemolytic *Staphylococcus albus* was found in 2 instances and a hemolytic streptococcus in 5. However, the hemolytic streptococcus was the sole pathogen in only 1 patient. The group of 75 patients differed from the first in two particulars. In the first place, the infections were much more chronic when first seen, and the patients had been treated unsuccessfully in from one to four general hospitals. Secondly, penicillin, in various doses and methods of administration, had been given to approximately 75 per cent of the patients. The sensitivity of the organisms to penicillin was determined by the filter paper technic, which will be discussed briefly in a later section.

Cultural studies revealed that the causative organisms in 75 per cent of the infections were insensitive to penicillin in a strength of 2 units per cubic centimeter. It should be emphasized at this point that sensitivity to penicillin in a strength of 2 units per cubic centimeter does not represent the amount of penicillin per cubic centimeter of agar, as was the case in the agar trench method. It represents, instead, the concentration of the penicillin solution which is used to moisten the disks of filter paper. Since an individual filter paper as used in this survey absorbed approximately 0.003 cc of solution, it is apparent that the disk moistened with this solution contained only a small fraction of a unit. However, as will be shown later, 500 units of penicillin per gram of ointment base proved effective only when the causative organisms were sensitive to penicillin in a concentration of not more than 2 units per cubic centimeter by the filter paper method. It follows, then, that the data on sensitivity for the earlier series are misleading and that the actual sensitivity of the organisms to penicillin would probably take place with a strength much less than 2 units of penicillin per cubic centimeter of agar. On the basis of a recent experiment with the pour plate method of penicillin assay and use of the Florey strain of *Staph aureus*, the true readings in most instances were probably in the region of  $\frac{1}{10}$  unit of penicillin per cubic centimeter of agar.

The question was then raised as to whether or not cure could be obtained when penicillin sensitivity tests revealed that the test organisms were sensitive to penicillin only in concentrations greater than 2 units per cubic centimeter by the

filter paper method. On testing with serial strengths of penicillin, it was found that the sensitivity of the organisms in different patients varied from sensitivity to 1 unit per cubic centimeter to insensitivity to 2,000 units per cubic centimeter, while the control Florey strain of *Staph aureus* remained uniformly sensitive at 1 to 2 units per cubic centimeter. As the study progressed, it became apparent that only in the patients with sensitivity to penicillin in concentrations of less strength (from 1 to possibly 20 units per cubic centimeter) could cures be obtained with the concentrations of penicillin used ordinarily in treatment. Of the group of 75 patients, the causative organisms were sensitive to penicillin in this range in 64 per cent. It seemed important, therefore, to determine the response of this comparatively large group to varying doses of penicillin administered both locally and systemically and given with or without supplemental therapy with sulfonamide compounds.

#### RESULTS OF TREATMENT

*Treatment with Penicillin Ointment in Strength of 500 Units per Gram*—Treatment for the first 20 patients consisted of the use of an ointment containing 500 units of sodium penicillin per gram of ointment base. The penicillin was dissolved in a small amount of distilled water and incorporated in a water-soluble ointment base, composed of 15 per cent Lanette wax and 15 per cent petrolatum in water. The ointment base was not sterilized, since in the previous series an aseptic technic did not result in a greater percentage of cures. The 20 patients were unselected and included those with all types of pyoderma. Moreover, the causative organisms were sensitive to penicillin in concentrations ranging from 1 to 2,000 units per cubic centimeter.

When the causative organisms were sensitive to penicillin in a strength of 1 to 2 units per cubic centimeter, cure was invariable, regardless of the nature of the presenting cutaneous infection. If the organisms were sensitive only to concentrations of penicillin greater than 2 units per cubic centimeter cure did not occur. For a patient with infectious eczematoid dermatitis, the organisms of which were sensitive to penicillin in a strength of 8 units per cubic centimeter, clinical arrest was obtained on two occasions, but relapse occurred promptly after discontinuance of therapy. In a second patient, with sycosis vulgaris and with organisms sensitive to penicillin in a strength of 8 units per cubic centimeter, there was a temporary improvement of 30 per cent, but this was followed by clinical progression. A third, with infectious eczematoid dermatitis with organisms sensitive to penicillin in a strength of 50 units per cubic centimeter, showed only transient improvement. In the remaining patients, in whom the causative organisms were sensitive to penicillin within a range of 10 to 2,000 units per cubic centimeter, no improvement was seen.

*Treatment with Penicillin Ointment in Concentrations Greater than 500 Units per Gram*—Varying concentrations of penicillin were used on a group of 15 patients in whom the organisms were sensitive to penicillin in concentrations ranging from 4 to 2,000 units per cubic

centimeter Penicillin ointment containing 1,660 units per gram was used for 3 patients, 1 with impetigo and 2 with infectious eczematoid dermatitis, with the organisms sensitive to penicillin in strengths of 10, 50 and 100 units per cubic centimeter, respectively. None of these patients was improved after two weeks of therapy. One patient with impetigo, with the organisms sensitive to penicillin in a concentration of 2,000 units per cubic centimeter was not improved by penicillin ointment containing 3,330 units per gram. One patient with chronic sycosis, the organisms of which were sensitive to penicillin in a dilution of 100 units per cubic centimeter, was unimproved after use of penicillin ointment containing 3,330 units per gram.

- The next 2 patients were of special interest. In the first a severe infectious eczematoid dermatitis of the face had developed some two months previously with a residual treatment-resistant sycosis of the bearded region. Culture yielded a coagulase-positive hemolytic *Staph aureus*, sensitive to 50 units of penicillin per cubic centimeter. Treatment was instituted with penicillin ointment, 10,000 units per gram, three times daily, but no improvement ensued after six days, at which time a repeated culture showed that the organisms had become resistant to penicillin in a strength of 500 units per cubic centimeter. A similar resistance was noted in the second patient, who had an acute pustular folliculitis of the legs. The causative organism was a coagulase-positive hemolytic *Staph aureus*, sensitive to penicillin in a strength of 20 units per cubic centimeter. The lesions persisted after thirteen days of therapy with penicillin ointment, 10,000 units per gram, and a second test showed that the organisms had become resistant to 500 units of penicillin per cubic centimeter. The facts observed in these 2 patients demonstrate that even massive penicillin therapy may be inadequate and predispose to the development of increased resistance to penicillin when the initial resistance of the organisms to penicillin is relatively high. They also confirm earlier observations<sup>1</sup> that both clinical and laboratory evidence of resistance to penicillin may develop in the course of a few days.

Three patients with chronic impetigo and 1 with long-standing multiple ecthymatous lesions, all due to coagulase-positive hemolytic staphylococci with sensitivity to penicillin in a strength of 4 units per cubic centimeter, were treated. Therapy consisted in administration of penicillin ointment, 3,000 units per gram, and all patients were cured within a ten day period.

The staphylococcic infections of 3 patients showed laboratory evidence of sensitivity to penicillin in dilutions of 6, 8 and 10 units per cubic centimeter, respectively. The first had an infectious eczematoid dermatitis of the face of eight months' duration. The process was arrested temporarily during three previous hospitalizations with the use



of penicillin ointment (500 units per gram), but there was invariably a relapse from seven to fourteen days after therapy was stopped. Culture revealed a coagulase-positive hemolytic *Staph albus*, sensitive to penicillin in a strength of 6 units per cubic centimeter. Treatment was instituted with an ointment containing 5,000 units of penicillin per gram, and complete involution occurred after two weeks of therapy. Treatment was then continued for another two weeks to insure permanency of results. The second patient had a subacute infectious eczematoid dermatitis involving the canal, tragus and lobule of the left ear. A coagulase-positive hemolytic *Staph aureus*, sensitive to 8 units of penicillin per cubic centimeter, was found on culture. Penicillin ointment, in a strength of 7,500 units per gram, was prescribed, and cure took place in six days. The last patient in the group had a treatment-resistant impetiginous and pustular infection of the finger of some thirty days' duration. Culture yielded a coagulase-positive *Staph aureus*, sensitive to penicillin in a strength of 10 units per cubic centimeter. Penicillin ointment, in a strength of 10,000 units per gram, was administered, and cure occurred in one week.

The last patient in this group had been hospitalized almost continuously for the preceding eight months because of a treatment-resistant sycosis vulgaris. Three million units of penicillin had been administered intramuscularly in eight separate courses, and penicillin ointment had been used for three weeks without effecting any improvement. On culture a coagulase-positive hemolytic *Staph aureus* was found, with sensitivity to penicillin in a strength of 20 units per cubic centimeter. Penicillin ointment in a strength of 100,000 units per gram was used and cure was accomplished with three days of therapy. In all, treatment was continued for five days, and there was not the slightest evidence of local irritation. The patient was followed for another month, but relapse did not occur.

*Treatment with Penicillin Ointment in Conjunction with Intramuscular Injections of Penicillin or with Intramuscular Injections Alone*

—Few of the patients reported on in this paper were given penicillin intramuscularly at this station. Many had been so treated, however during previous hospitalizations, and in general the results were disappointing. Frequently, therapy had been administered without preliminary determination of sensitivity to penicillin, and 5 of these cases will be summarized later. The only obvious indication for intramuscular administration of penicillin in treatment of pyoderma is severe infectious eczematoid dermatitis in a widespread distribution. Furthermore the causative organisms should be sensitive to penicillin in a concentration of not more than 2 units per cubic centimeter by the filter paper method or, in general, as sensitive as the control Florey strain of *Staph aureus*. Two patients with widespread infectious eczematoid dermatitis were

treated with penicillin given intramuscularly, but the organisms were resistant to penicillin in both instances and improvement was not derived from penicillin therapy. Too much reliance should not be placed on intramuscular penicillin therapy, especially when the causative organisms are sensitive to penicillin only in concentrations of 4 or more units per cubic centimeter. This point was demonstrated conclusively by the case of the patient, previously mentioned, who received massive local penicillin therapy. It is also well illustrated by the following case report.

A soldier, aged 32, had severe sycosis of twenty years' duration, with resistance to all previous forms of therapy, including roentgen rays to the point of tolerance and sulfonamide compounds administered both locally and systemically. Culture yielded a coagulase-positive hemolytic *Staph aureus* which was sensitive to penicillin in a strength of 10 units per cubic centimeter. Prolonged therapy with penicillin was given, penicillin ointment in a strength of 500 units per gram being supplemented with 40,000 units given intramuscularly every three hours. Two courses of six days each were separated by a six day course of sulfadiazine, 90 grains (5.8 Gm) daily. Clinical arrest was obtained on this regimen and cultures taken from the normal skin during the next five months did not reveal pathogenic organisms. Nevertheless, a minor folliculopustular relapse ensued six months later, and a pathogenic *Staph aureus* was found which was sensitive to penicillin only in a concentration of 100 units per cubic centimeter.

In retrospect, it is probable that organisms (presumably lying dormant in hair follicles) whose growth had been retarded by the penicillin not only had again become active but also had developed an increased resistance to penicillin. Furthermore, on the basis of more recent study, it is apparent that the increased resistance to penicillin was engendered by inadequate doses of the drug. Satisfactory local concentrations of penicillin (as judged by clinical cure) cannot be obtained with the aforementioned regimen of treatment in cases of infections in which there is a sensitivity to penicillin in the strength of 10 units per cubic centimeter.

*Penicillin Supplemented by Sulfonamide Therapy* Rammelkamp and Keefer<sup>2</sup> have stated, on the basis of experimental studies, that penicillin and the sulfonamide compounds may act synergistically in the control of infections. They found that small amounts of penicillin, which alone had no inhibitory effect against staphylococci, would enhance the antistaphylococcus action of sulfathiazole in defibrinated whole blood. Clinical experimentation in cases of pyoderma, however, has shown that when the causative organisms are sensitive to penicillin in a concentration of not more than 2 units per cubic centimeter, local penicillin therapy alone almost invariably accomplishes permanent cure. Accordingly, the only reasonable field of usefulness of combined peni-

2 Rammelkamp, C. H., and Keefer, C. S. Penicillin Its Antibacterial Effect in Whole Blood and Serum for the Hemolytic *Streptococcus* and *Staphylococcus Aureus*, *J. Clin. Investigation* 22: 649 (Sept.) 1943.

cillin-sulfonamide therapy would seemingly be in the treatment of infections in which the organisms are sensitive to penicillin only in concentrations of 4 or more units per cubic centimeter. However, since penicillin ordinarily is a more potent antibacterial agent than are the sulfonamide compounds in the control of staphylococcic infections, best results in this type of case should be obtained by adequate concentrations of sulfonamide compounds and by concentrations of penicillin calculated from the results of penicillin-sensitivity tests.

Ten patients with treatment-resistant pyoderma with sensitivity to penicillin in dilutions varying from 4 to 20 units per cubic centimeter were treated with penicillin ointment, 500 units per gram, combined with 5 per cent sulfadiazine. The results were disappointing, and cure did not occur in a single instance. It is to be emphasized, however, that 8 of the 10 patients had previously used sulfadiazine ointment without improvement. Further studies, using increasing concentrations of penicillin with sulfadiazine, are now in progress, and results will be reported at a later date. Increasing local concentrations of sulfadiazine are not being used, because of the tendency to local irritation and secondary infectious eczematoid dermatitis.

In 4 cases it has appeared that two courses of penicillin locally, with an intervening course of sulfadiazine by mouth, have been of value in the management of infections moderately resistant to penicillin. In the aforementioned patient, however, relapse finally ensued, and the necessity of an adequate concentration of penicillin cannot be overstressed. The potential value of the penicillin-sulfadiazine-penicillin sequence has been further confirmed by study of the following case.

A soldier, aged 26, with a noncontributory past history, had a chronic, intermittently infectious, eczematoid dermatitis of the left wrist for six years. Four months before he was admitted to the hospital the lesions again became infected, spread locally and to the right hand and were soon complicated by a severe lymphangitis extending to the right axilla. After temporary improvement the dermatitis relapsed, and the lymphangitis became clinically manifest in both upper extremities. Some 500,000 units of sodium penicillin had been administered intramuscularly without improvement. On the patient's admission to the hospital, a coagulase-positive hemolytic *Staph aureus* resistant to penicillin in a strength of 50 units per cubic centimeter was found. The lymphangitis and pyoderma persisted despite continuous soaks, and, accordingly, sulfadiazine was administered, 75 grains (4.8 Gm) daily for eleven days. The lymphangitis began to recur on the eleventh day of sulfonamide therapy, the organism was restudied and was found to have become sensitive to penicillin in a dilution of 4 units per cubic centimeter. Therapy with penicillin applied locally, in a dosage of 3,000 units per gram of ointment supplemented by 40,000 units administered intramuscularly every three hours, was begun. The lymphangitis and the pyoderma were cured with five days of therapy, a residue of low grade eczematoid dermatitis being left.

*Penicillin in Combined Staphylococcic and Streptococcic Pyoderma*  
—Four patients in the present series had combined hemolytic staphylo-

coccus and streptococcus infections. Three of these had infectious eczematoid dermatitis, and the fourth had ecthyma. In the first 2, the hemolytic staphylococci found were insensitive to 100 and to 2,000 units of penicillin per cubic centimeter, respectively, and penicillin was not used, although the streptococci were sensitive to 1 unit per cubic centimeter. The third patient, with both organisms sensitive to 10 units of penicillin per cubic centimeter, failed to improve with penicillin ointment containing 500 units per gram. The last one, with a severe infectious eczematoid dermatitis, was interesting because of the fact that the infection was largely streptococcic in nature and clinical differentiation of the staphylococcic and streptococcic components was possible. The hemolytic streptococcus was sensitive to 1 unit of penicillin per cubic centimeter while the coagulase-positive, hemolytic staphylococcus was insensitive to 10 units per cubic centimeter. The streptococcic lesions cleared in three days with penicillin ointment in a strength of 500 units per gram, while those due to staphylococci persisted and required potassium permanganate baths and ammoniated mercury for their involution.

*Penicillin in Aqueous Solution* Penicillin has been used occasionally in the form of aqueous solutions, in a strength of 25 to 200 units per cubic centimeter for exudative infectious eczematoid dermatitis. In general, this treatment is not to be recommended, for the amount of penicillin necessary to maintain an adequate concentration in continuous wet compresses is prohibitively large. In addition, the sodium salt may be irritating to the tissues, especially when a superimposed overtreatment or contact dermatitis from other agents has occurred. These points are illustrated by the following case.

A soldier, aged 31, had an infectious eczematoid dermatitis of the hands. Local treatment during a three month period included use of solution of aluminum acetate and ointments of chrysarobin, sulfur and salicylic acid, tar and sulfadiazine, all aggravating the eruption. Penicillin soaks, in a strength of 25 units per cubic centimeter, were then given for a two week period, with considerable aggravation of the eruption and no improvement of the pyoderma. On the patient's admission to the hospital, a severe chemical dermatitis and pyoderma were present. Culture revealed a coagulase-positive hemolytic *Staph aureus* sensitive to penicillin in a dilution of 10 units per cubic centimeter. Patch tests with a solution of penicillin and with penicillin ointment elicited negative reactions.

In retrospect, it is apparent not only that the infection was insensitive to sodium penicillin in the concentration used but also that a local irritating effect from the preparation had supervened.

*Use of Penicillin in Miscellaneous Conditions* Penicillin has been of little value against furunculosis, secondarily infected acne or infected sebaceous cysts, whether given topically, intramuscularly or by local injection into circumscribed lesions. Temporary improvement of chronic extensive furunculosis has been followed by complete relapse even when

the organisms are sensitive to penicillin in concentrations not exceeding 1 unit per cubic centimeter. General tonic measures and the use of staphylococcus toxoid are to be preferred. In cases of secondarily infected acute dermatophytosis, penicillin may cause an exacerbation of the lesions, even when the organisms responsible for the secondary infection are sensitive to penicillin. This phenomenon may be due to the action of penicillin on tissues sensitized to the fungi causing the ringworm infection, for it is known that a common antigenic substance is present in all fungi. Personal study of reactions to penicillin has suggested that penicillin contains this common antigen.

Penicillin is useful for secondarily infected eczematous dermatoses, but, as stated<sup>1</sup> before, its effect is solely that of an antibacterial agent. No improvement can be expected in the underlying dermatosis, except so far as the dermatosis has been aggravated by the infection.

*Empiric Use of Penicillin Therapy*—The question as to whether or not penicillin therapy should be used empirically in cases of severe cutaneous infections may be answered by the following case reports.

A soldier, aged 23, was hospitalized because of an acute infectious eczematoid dermatitis of the face. A test for sensitivity to penicillin was made, but because of the severity of the infection local and intramuscular penicillin therapy was instituted. The eruption became decidedly worse in the following two days, with the development of diffuse cellulitis of the head and autosensitization, eczematous lesions over the body. Culture revealed a hemolytic *Staph aureus*, insensitive to penicillin. Colloid baths, continuous soaks with isotonic solution of sodium chloride and soothing topical measures were then prescribed, with gradual involution taking place over a thirty day period. In this case, the ineffectiveness of penicillin was responsible for a dangerous progression of the infection.

A soldier, aged 19, had been bothered with approximately one hundred furuncular lesions over a period of six months. Penicillin intramuscularly had been given on two occasions, 500,000 units in a five day period two months after the onset and 360,000 units in a three day period two months later. Hot soaks of solution of boric acid were used during both courses of treatment. Temporary improvement occurred after each course of penicillin, but after two weeks a complete relapse supervened. On the patient's admission to the hospital, the furunculosis was present in its original severity. Culture yielded a hemolytic *Staph aureus* sensitive to penicillin only in a concentration of 20 units per cubic centimeter. A moderate degree of secondary anemia was found. Permanent arrest was obtained after the use of iron, extract of liver, ultraviolet irradiation, multivitamin capsules and a course of staphylococcus toxoid. In this case it is apparent that penicillin could exert no more than a temporary ameliorative effect with the tissue concentration obtained with intramuscular injections, furthermore, the background of lowered resistance would not be altered.

A soldier, aged 25, had a long-standing, intermittently recurrent, nummular eczema of the distal extremities, on which a secondary infectious eczematoid dermatitis had recently developed. The use of ointment of tar improved the eczema but aggravated the pyoderma, and penicillin soaks, 25 units per cubic centimeter, were used for one month, to a total dosage of approximately 500,000 units. No improvement was obtained, and he was referred to this station. On culture, a coagulase-positive hemolytic *Staph aureus*, sensitive to penicillin in a

concentration of 20 units per cubic centimeter, was found. The degree of resistance to penicillin encountered in this patient is a definite contraindication to the use of penicillin intramuscularly or locally in the concentrations used in this case.

A soldier, aged 26, was hospitalized because of a severe infectious eczematoid dermatitis and cellulitis involving the face, neck and scalp. Treatment consisted of continuous wet packs and penicillin administered intramuscularly for nine days, to a total of 960,000 units. Gradual improvement ensued, but because of the persistence of the infection penicillin soaks, in a concentration of 25 to 100 units per cubic centimeter, were applied for a two week period. A total of 600,000 units of penicillin was used but without improvement, and the patient was evacuated to this station. Culture revealed a coagulase-negative hemolytic *Staph aureus*, insensitive to penicillin in a concentration of 2,000 units per cubic centimeter, and a hemolytic streptococcus, sensitive to penicillin in a dilution of 1 unit per cubic centimeter. The persistence of this infection was due to the reliance on penicillin for the destruction of an organism which was completely resistant to penicillin. The patient made an uneventful recovery in two weeks with boric acid compresses and 3 per cent ammoniated mercury ointment.

A soldier, aged 43, had been treated for a severe sycosis vulgaris with penicillin intramuscularly, in a total dosage of 2,400,000 units. A severe sensitization reaction to penicillin, consisting of generalized urticaria and angioneurotic edema, then supervened, and penicillin therapy was stopped. On the patient's admission to the hospital, ten days later, the reaction had practically cleared, but the sycosis was unimproved. On culture, a coagulase-negative hemolytic *Staph aureus*, insensitive to penicillin in a concentration of 2,000 units per cubic centimeter was found.

This case not only emphasizes the wastage of time and penicillin in a completely penicillin-resistant infection but also brings up the important point that severe reactions may result from the use of penicillin. In a recent study, Cormia, Jacobson and Smith<sup>3</sup> found that severe reactions to penicillin occur in 0.5 per cent of patients given prolonged courses. These reactions included severe urticaria, complicated at times by angioneurotic edema, shock, pulmonary edema and convulsions. Acute syncope and serum-sickness-like syndromes were observed. Various types of erythematovesicular eruptions occurred, in some of these, areas which had been the sites of a previous active dermatophytosis or dermatophytid were involved. It is apparent that the administration of penicillin not only is a time-consuming, exact and expensive procedure but also may be complicated by severe reactions. The careful selection of patients for treatment is therefore of the greatest importance.

#### LABORATORY CONTROL IN MANAGEMENT OF PYODERMA

The filter paper method, because of its convenience, was used for the determination of sensitivity to penicillin in most of the cases. In this method the test organisms were streaked across a blood agar plate and the control organisms across another. Disks of filter paper, 6 mm in diameter, were then saturated with varying dilutions of penicillin solu-

<sup>3</sup> Cormia, F. E.; Jacobson, L. Y., and Smith, E. L. Reactions to Penicillin, *Bull. U. S. Army M. Dept.* 4:694 (Dec.) 1945.

tion and placed on the plates. The sensitivity or resistance of the organisms was determined by comparing the two plates. A strain of the Florey Staph aureus, maintained in nutrient broth at room temperature, was used as the control. This organism occasionally developed an increased resistance to penicillin, when this occurred the original degree of sensitivity was restored by passage on a blood agar plate followed by inoculation into fresh broth. From time to time the test solutions of penicillin diminished in potency after standing for more than a week, this difficulty was averted by the use of fresh penicillin solutions for each test.

As the study progressed, it became apparent that there were more variations in the results than were warranted by variations in the control organism. It was found that the amount of penicillin solution absorbed on the filter paper when the edge of the paper was dipped into the solution had a possible range of variation of from 0.002 to 0.004 cubic centimeters. Accordingly, it seemed advisable to check the method against one in which the amounts of penicillin solution used were carefully titrated for each test. The control method was that devised by Cooke.<sup>4</sup> In this method an area 2 by 5 cm. is marked off on the bottom of an agar plate, and then exactly 0.1 cubic centimeter of the test penicillin solution is pipetted evenly over the agar within the marked area and dried quickly in the refrigerator. The organisms to be tested are then streaked across the area, and the inhibition of growth or its absence is noted as usual.

In 20 cases tested by both methods, a rough correlation in the results was observed. The control organism was routinely inhibited by 0.03 unit of penicillin per 0.1 cubic centimeter by the Cooke method and by 2 units per cubic centimeter by the filter paper method. There was, however, a distinct tendency for the results by the filter paper method to assay lower than those by the direct method, the ratio being roughly 3 to 1. While this fact in no way invalidates the conclusions drawn in this paper, it may indicate that the proper dosage of penicillin for local therapy is even higher than is suggested in this report. In the future this difficulty may be avoided by exact titration of the amount of solution used in each test, regardless of the method used. Other factors which must be kept constant are the size of the disk, the depth of the agar in the plate and the temperature and duration of incubation. The number of bacteria in the inoculum, said by Sherwood and her associates<sup>5</sup> to influence the final results, was not considered in the present observations.

<sup>4</sup> Cooke, J. V. A Simple Clinical Method for the Assay of Penicillin in Body Fluids and for the Testing of Penicillin Sensitivity of Bacteria, *J. A. M. A.* **127** 445 (Feb. 24) 1945.

<sup>5</sup> Sherwood, M. B., Falco, E. A., and de Beer, E. J. A Rapid, Quantitative Method for the Determination of Penicillin, *Science* **99** 247 (March 24) 1944.

## COMMENT

The results of the present study suggest that the optimum method of administering penicillin in treatment of cutaneous infections is by topical applications of the substance in a water-soluble ointment base. The ointment has many advantages over solutions, whether used locally or parenterally. It is more economical, the penicillin stays in contact with the affected area for a longer period, and much greater local concentrations of penicillin can be attained by application of the ointment than by intramuscular injections.

The importance of performing a test for sensitivity to penicillin prior to the institution of treatment cannot be overemphasized. The results of the sensitivity test proved to be a valuable guide for the use of penicillin therapy. The concentration of penicillin in the ointment should be varied according to the degree of sensitivity of the causative organisms to penicillin. A strength of 500 units per gram

*Strength of Penicillin Ointment to Be Used in Treatment According to Sensitivity of Organisms to Penicillin*

Sensitivity of Organism		Strength of Penicillin Units per Gram of Ointment
Filter Paper Method, Units per Cc	Cooke Method, Units per 0.1 Cc	
1	0.03 to 0.06	500
2	0.1	1,000
4	0.15	3,000
6	0.2	5,000
8	0.25	7,500
10 to 20	0.3 to 0.6	10,000 to 25,000 (?)
20 to 30	0.6 to 1	25,000 to 50,000 (?)
30 to 50	1 to 2	100,000 (?)

was found satisfactory when the organism was sensitive to penicillin in a concentration not greater than 2 units per cubic centimeter by the filter paper method. Preliminary experiments have shown that when the sensitivity ranges from 4 to 10 units per cubic centimeter cure may occur when the strength of the ointment is sufficiently increased. However, the exact concentrations to be used in a given case will have to be determined by further study. The schedule recommended tentatively for additional clinical investigation is shown in the table.

The routine of treatment consisted of preliminary application of hot boric acid packs for twenty minutes, removal of crusts and opening of pustules, followed by application of the ointment. Treatment was administered twice daily when the organisms were sensitive to 1 to 2 units of penicillin and three times daily when they were sensitive to 4 or more units. In the earlier work<sup>1</sup> penicillin therapy was continued for three to five days after clinical involution took place.



On the basis of the present study, however, it is felt that the length of treatment after involution should be five days in cases of simple pyoderma and up to two weeks in cases of slowly clearing or relapsing infections. In this series, prolongation of therapy has not been followed by an appreciable increase in sensitization reactions.

The frequency of natural resistance of the *Staph aureus* to penicillin has not been definitely established. The causative organisms in 22.5 per cent of patients treated in the earlier series<sup>1</sup> were initially resistant to penicillin, while the organisms in an additional 15 per cent became resistant as a result of inadequate penicillin therapy. The high percentage of organisms resistant to penicillin encountered in this series (75 per cent) was thought to be due partly to intrinsic resistance of the organisms, with filtering of the cases through various treatment centers to this station, and partly to developing resistance as a result of previous inadequate penicillin therapy. Analysis of previous treatment disclosed that in some instances short courses of penicillin intramuscularly had been given while in others penicillin was incorporated in an inert type of base, such as cold cream or petrolatum. In an additional group, an inadequate concentration of penicillin, such as 200 units of penicillin per gram of ointment base, was used.

It was impossible to predict the development of resistance to penicillin from the results of initial sensitivity tests. It is probable that resistance is more likely to develop when the organisms are initially sensitive to penicillin in a strength of more than 2 units per cubic centimeter. Increased resistance to penicillin is undoubtedly provoked by inadequate doses regardless of the method of administration. On the basis of former observations<sup>1</sup> and of several cases studied in the present series, there is some suggestion that an intervening course of a sulfonamide compound may alter favorably the response of staphylococcic pyoderma to penicillin, conversely, it is possible that an intervening course of penicillin may affect similarly the reaction of the infection to the sulfonamide compounds.

Resistance of the organisms to penicillin was not of unfavorable prognostic significance so far as cure by other methods of treatment was concerned. The development of resistance to penicillin may be avoided for the most part by an adequate concentration of penicillin in a water-soluble ointment base and by continuation of treatment for at least five days after clinical involution occurs.

Penicillin is a valuable adjunct in the treatment of pyoderma but should be used only in carefully selected cases. Moreover, since many infections do not respond to penicillin, standard methods of treatment often must be used.

SUMMARY

1 Penicillin is a valuable adjunct in the management of treatment-resistant pyoderma.

2 Penicillin should never be administered for pyoderma unless a test for sensitivity to penicillin has been made

3 The best method of administration of penicillin for pyoderma is by local applications in a water-soluble ointment base

4 A concentration of 500 units of penicillin per gram of ointment is efficacious when the causative organisms are sensitive to penicillin in a concentration of not more than 2 units per cubic centimeter by the filter paper method and 0.1 unit per 0.1 cubic centimeter by the Cooke method

5 When the causative organisms are sensitive to penicillin only in concentrations greater than those mentioned in paragraph 4, the amount of penicillin in the ointment should be appropriately increased

6 Supplementary therapy with sulfonamide compounds has been of limited value in this series

7 Inadequate dosage and short periods of administration of penicillin are believed to predispose to the development of resistance to penicillin

## ETIOLOGIC CONSIDERATIONS OF KERATOSIS BLENNORRHAGICA

Report of a Case in Which Penicillin Was Used

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SINCE the first case report of keratosis blennorrhagica, by Vidal in 1892, this comparatively rare disease has been discussed thoroughly by a great number of authors

Half a century of literature based on the pathologic investigation and observation of well over 100 cases has clarified many aspects of the disease and has brought out data and facts which are now generally accepted. Most authors seem to agree today on its morphologic aspects, on its incidence and on its relation to age, to sex and to other gonorrheal complications. However, there is great uncertainty and considerable disagreement concerning the pathogenesis of the disease. While gonorrheal infection is accepted by most of the authors as the primary etiologic factor, there still remain unanswered questions that are open for further inquiry and discussion.

To facilitate such investigation and discussion we wish to restate certain facts already known and to tabulate the data gleaned out of the literature of fifty years. Using as a point of departure the excellent chapter of Buschke and Langer<sup>1</sup> on gonorrheal dermatoses, which covers the literature up to 1926, and Langer's chapter in the *Handbuch*,<sup>2</sup> we have collected reference material on the subject from 1927 to the present.

### INCIDENCE

We have found 108 cases of gonorrheal keratosis reported in the literature since 1927. Adding to this number the 57 cases collected by Buschke and Langer, plus our following case report, there have been 166 cases reported in the entire literature to our knowledge. This figure is greatly at variance with the figures of other authors, shown in table 1.

1 Buschke, A., and Langer, E. *Lehrbuch der Gonorrhoe*, Berlin, Julius Springer, 1926.

2 Langer, E. *Hautkrankheiten bei Gonorrhoe*, in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1930, vol. 22, pt. 2, pp. 40-71.

Our figure of 166 cases does not include the cases reported as keratosis blennorrhagica without gonorrhea or as Reiter's disease with keratosis. We have found 28 such case reports since 1927 and about 34 references in the entire literature. Mastrojanni<sup>3</sup> in 1936 mentioned 10 such cases, including his own. Some of these cases, however, may easily be interpreted as instances of gonorrheal keratosis, in spite of the lack of microscopic and cultural evidence.

According to the present consensus there is no sharp dividing line between the various types of gonorrheal exanthemas and gonorrheal keratosis, some cases reported as instances of hemorrhagic, vesicular, urticarial or other exanthemas may fall into the category of cases of keratosis blennorrhagica. We have to assume, therefore, that these figures are far from representing the actual incidence of keratosis blennorrhagica and other gonorrheal exanthemas, as the number of

TABLE 1—*Number of Cases of Gonorrheal Keratosis Reported by Various Authors*

Author	Year	Number of Cases
Simpson <sup>22</sup>	1912	20
Haase <sup>66</sup>	1916	30
Keim <sup>69</sup>	1924	59
Buschke and Langer <sup>1</sup>	1926	57
Willmott <sup>134</sup>	1926	65
Mills, E. R. Urol & Outan Rev 31 418, 1927	1927	70
Scomazzoni <sup>7</sup>	1931	90
Downing <sup>30</sup>	1934	83
Oombes, Dietrich and Cohen <sup>20</sup>	1940	93
Rajam and Rangiah <sup>27</sup>	1941	93

unreported cases must be considerable. Nevertheless, we can safely conclude that keratosis blennorrhagica is a rare disease but perhaps not quite so rare as was formerly believed.

Arning and Meyer-Delius<sup>4</sup> found in 4,850 cases of gonorrheal infection 159 cases of arthritis and 6 cases of keratosis. Harrison<sup>5</sup> found 1 case of keratosis in 5,000 cases of gonorrhea. Brown and Hargreaves<sup>6</sup> reported a ratio of 1/7,500. Scomazzoni<sup>7</sup> found 2 cases of keratosis in 11,000 cases of gonorrheal infections, a ratio of 1/5,500.

The age of the patients reported with keratosis blennorrhagica was predominantly in the fourth decade. Many of them were in their

3 Mastrojanni, D. Contributo allo studio della poliartrite ipercheratolica infettiva, Arch ital di dermat, sif 12:105, 1936.

4 Arning, E., and Meyer-Delius, H. Beitrag zur Klinik der gonorrhoeischen Hyperkeratosen, Arch f Dermat u Syph 108.3, 1911.

5 Harrison, L. W. Venereal Disease in General Practice, London, Oxford University Press, 1918.

6 Brown, W., and Hargreaves, H. A Case of Gonorrheal Keratosis, Brit J Dermat. 29:107, 1917.

7 Scomazzoni, T. Considerazioni sulla patogenesi della cheratoderma blennorrhagica, Gior ital di dermat e sif 72:716, 1931.

twenties, a few in their forties and some in other age groups. Three cases of children 5 to 7 years of age with typical lesions of keratosis were reported, their primary disease was gonorrheal vulvovaginitis (Langer,<sup>2</sup> Louste and Levy-Franckel<sup>8</sup>). The disease mainly affects the male sex, a curious fact never yet explained. We have found 10 cases of keratosis blennorrhagica affecting women (Robert,<sup>9</sup> Levy-Franckel,<sup>10</sup> Isaac,<sup>11</sup> Lees,<sup>12</sup> Buschke and Langer,<sup>13</sup> Beatty,<sup>14</sup> Kristjanssen,<sup>15</sup> Finlay,<sup>16</sup> Wayson<sup>17</sup> and Goldman<sup>18</sup>), a ratio of 1 woman to every 15.3 male patients. Among the patients reported with keratosis without gonorrhea or with Reiter's disease with keratosis 4 were women and 30 were male patients. Of the 25 patients reported since 1927 as having gonorrheal exanthemas without keratosis, 21 were men, 2 were women and 2 were infants.

#### SYMPTOMATOLOGY AND CLINICAL COURSE

First described by Vidal<sup>19</sup> (1892) in France, Buschke<sup>20</sup> (1899) in Germany, Turnbull and Sequeira<sup>21</sup> (1910) in England and Simpson<sup>22</sup> (1912) in America, the clinical characteristics of keratosis blennorrhagica

8 Louste, A., and Levy-Franckel, A. Keratose blennorrhagique chez une fillette de cinq ans, *Bull Soc franç de dermat et syph* **37** 362, 1930

9 Robert, E. Contribution a l'etude des troubles trophiques cutanees dans la blennorrhagie, Thesis, Paris, no 300, 1897

10 Levy-Franckel, A. Keratodermie blennorrhagique, *Ann d mal ven* **13** 385, 1918

11 Isaac, C. L. A Case of Keratodermia Blennorrhagica in a Woman, *Brit J Dermat* **32** 195, 1920

12 Lees, D. Keratodermia Blennorrhagica, *Edinburgh M J* **28** 99, 1922

13 Buschke, A., and Langer, E. Hyperkeratotische Exantheme bei Gonorrhoe und ihre Beziehungen zur Psoriasis, *Dermat Wchnschr* **76** 145, 1923

14 Beatty, J. Symmetrical Hyperkeratosis of Extremities (Keratodermia Blennorrhagica), *Brit M J* **1** 14, 1927

15 Kristjanssen, A. Gonorrhoeische Keratosen, *Zentralbl f Haut- u Geschlechtskr* **29** 257, 1929

16 Finlay, D. E. Keratodermia Blennorrhagica, *Brit M J* **1** 979, 1931

17 Wayson, J. T. Keratoderma Blennorrhagicum, *Arch Dermat & Syph* **24** 291 (Sept) 1931

18 Goldman, B. A. Keratodermia Blennorrhagica. Report of Cases, *Pennsylvania M J* **37** 299, 1934

19 Vidal, E. Éruption generalisee et symetrique de croûtes cornees avec chute des ongles d'origine blennorrhagique, coincidant avec une polyarthrite de même nature recidive a la suite d'une nouvelle blennorrhagie deux ans apres la guerison de la premiere maladie, *Ann de dermat et syph* **4** 3, 1893

20 Buschke, A. Ueber Exantheme bei Gonorrhoe, *Arch f Dermat u Syph* **48** 181 and 385, 1899

21 Sequeira, J. H. Case of Keratodermie Blennorrhagique, *Proc Roy Soc Med* **3** 77, 1909-1910

22 Simpson, F. E. Keratodermie blennorrhagique, *J A M A* **59** 657 (Aug 24) 1912

have been discussed in excellent papers by Arning and Meyer-Delius,<sup>4</sup> Chauffard and Fiessinger,<sup>23</sup> Buschke and Langer,<sup>1</sup> Lees and Percival,<sup>24</sup> Taylor,<sup>25</sup> Combes, Dietrich and Cohen,<sup>26</sup> and Rajam and Rangiah<sup>27</sup>

The salient clinical points are as follows. Keratosis blennorrhagica is the cutaneous manifestation of a grave systemic disease. The systemic manifestations are always preceded several days, weeks or months by the onset of urethritis, proved gonorrheal in a majority of the cases. Prostatitis and inflammation of the seminal vesicles are also commonly present. Swelling and pain of several joints in succession or simultaneously follow, preceding the onset of cutaneous lesions. The swelling and redness are not severe, however, the pain may be excruciating and the motility of joints limited. Four cases of keratosis without arthritis were reported by Jones,<sup>28</sup> Scholtz,<sup>29</sup> Downing<sup>30</sup> and Morita.<sup>31</sup> A large number of the patients have had a history of several previous or successive attacks of gonorrhea, arthritis and keratosis developing with each relapse or reinfection. In several cases reported as instances of nongonorrheal disease or as Reiter's disease, a history of 1 or more attacks of urethritis associated with inflammation of the adnexa following shortly after intercourse was at least highly suggestive of a latent gonorrheal focus. In some cases the onset of the syndrome followed immediately the passing of sounds or other urethral manipulations in an apparently nongonorrheal patient who, however, had a history of previous gonorrheal infection (Finger,<sup>32</sup> Lewin,<sup>33</sup> Langer,<sup>2</sup> Malherbe,<sup>34</sup>

23 Chauffard, A, and Fiessinger, N. Deux cas de keratose blennorrhagique, reproduction expérimentale de la lésion cutanée, *Bull Soc franç de dermat et syph* 20 162, 1909

24 Lees, D, and Percival, G. H. Keratoderma Blennorrhagica, *Lancet* 2 1116, 1931

25 Taylor, N. S. Keratoderma Blennorrhagicum, *Brit J Dermat* 51 418, 1939

26 Combes, F. C., Dietrich, C., and Cohen, J. Keratosis Blennorrhagica, *J A M A* 114 2078 (May 25) 1940

27 Rajam, R. V., and Rangiah, P. N. Keratoderma Blennorrhagica, *Indian M Gaz* 1 468, 1941

28 Jones, T. R. L. Unusual Case of Hyperkeratosis Blennorrhagica, *Brit M J* 1 153, 1929

29 Scholtz, M. A Syndrome of Blennorrhagic Keratoderma, *Arch Dermat & Syph* 15.165 (Feb) 1927

30 Downing, J. G. Keratoderma Blennorrhagicum, *Arch Dermat & Syph* 23 760 (April) 1931, *J A M A* 102 829 (March 17) 1934

31 Morita, S. Case of Keratoderma Plantare in a Gonorrhea Case, *Jap J Dermat & Urol* 36 31, 1934

32 Finger, E. Purpura rheumatica als Komplikation blennorrhagischer Prozesse, *Wien med Presse* 21 961, 1880

33 Lewin, G. Erythema exsudativum multiforme, *Charité-Ann* (1876) 3-622, 1878

34 Malherbe. Urethrites a gonocoques recidivantes, arthropathies multiples, troubles trophiques cutanées, cornes, *Gaz méd de Nantes*, 1901, vol 16, no 6

and Sullivan <sup>35</sup>) The onset of the exanthema, which usually follows the onset of arthritis, is sudden and is associated with chills and fever Within a few days large areas of the skin may be involved, showing lesions in different stages of evolution The distribution of the cutaneous lesions is symmetric, with a predilection for the feet, soles, ankles and hands, the areas around the involved joints and the genitals The lesions have been less frequently observed on the scalp, the trunk and the mucous membranes of the mouth They may be widely disseminated or may be localized only on the extremities (Baermann) A number of cases were reported with localization only on the penis, a clinical picture called "balanitis circinata sicca" (Arning and Meyer-Delius,<sup>4</sup> Jeanselme and Blamontier,<sup>36</sup> Baermann,<sup>37</sup> Chauffard and Fiessinger,<sup>23</sup> Jadassohn,<sup>38</sup> Blumenthal and Sherman,<sup>39</sup> Sherman, Blumenthal and Heidenreich,<sup>40</sup> Gadrat and Moiel <sup>41</sup> and Reiss <sup>42</sup>) The typical lesion begins as a pinhead-sized to lentil-sized hard vesicle surrounded with an erythematous halo It soon becomes a pustule with dry cheesy content After the pustule breaks open, losing its top, it forms a dirty brown, hard crust with an indurated corneous collar Interspersed among the lesions occasional papules, hemorrhagic bullae, and erythematous plaques can be observed

In the later stages of evolution there is an extensive coalescence of the mature lesions forming relief-map-like areas which may involve the whole sole or palm and large areas around the involved joints These confluent areas have a dusky red and slightly moist base and sharp, slightly raised margins and are covered with dry powdery scales This picture may predominate from the beginning on the genital and perineal regions with more or less oozing, showing a scarcity of typical vesicles or pustules The sharp margins, dusky red base and powdery or flaky scales may suggest a resemblance to psoriasis

35 Sullivan, S J Cutaneous Eruptions Accompanying Gonorrhea Report of a Case of Hemorrhagic Exanthema, *Urol & Cutan Rev* **38** 93, 1934

36 Jeanselme, E, and Blamontier Un cas de keratose blennorrhagique strictement localisee au gland, *Bull Soc franç de dermat et syph* **10** 493, 1922

37 Baermann, G Ueber hyperkeratotische Exantheme, *Arch f Dermat u Syph* **69** 363, 1904

38 Jadassohn, J Ueber infectiose und toxische hamatogene Dermatosen, *Berl klin Wchnschr* **37** 38, 1904

39 Blumenthal, F, and Sherman, W L Penile Blennorrhagic Keratoderma with Abortive Course, *Am J Syph, Gonor & Ven Dis* **22** 176, 1938

40 Sherman, W L, Blumenthal, F, and Heidenreich, J Blennorrhagic Balatiniform Keratoderma, *Arch Dermat & Syph* **39** 422 (March) 1939

41 Gadrat, J, and Morel, L Gonococcie severe avec arthropathies multiples, *Bull Soc franç de dermat et syph* **42** 1849, 1935

42 Reiss Urethralgonorrhoe, Balanitis gonorrhoeica, Arthritis gonorrhoeica, *Zentralbl f Haut- u Geschlechtskr* **37** 17, 1931

The toes and fingers show a diffuse, slightly moist, erythematous involvement of the last phalanges, on which firm pinhead-sized vesicles are scattered. These vesicles have a clear waxy content and do not enlarge or become real pustules before they break down. The picture is strongly suggestive of acrodermatitis perstans. The nails become dry and brittle, and may be lifted up from the nail bed by subjacent lesions and heaped-up corneous material.

The scalp, if involved, shows vesicles and papules on erythematous plaques which soon coalesce into moist scaly areas with a predilection for the hairline, a picture which strongly resembles seborrheic dermatitis. In the mouth, the lesions may be localized on the cheeks, on the tongue and especially on the hard and soft palate. These lesions are discrete flat lentil-sized papules with grayish keratotic borders sitting on erythematous bases. Their appearance follows closely the onset of the arthritis, and they disappear within a week or ten days. These oral lesions were reported in the cases of Stanislawski,<sup>43</sup> Frei,<sup>44</sup> Barrett,<sup>45</sup> Guerrieri,<sup>46</sup> Bogrow,<sup>47</sup> Sherman, Blumenthal and Heidenreich,<sup>48</sup> Berman,<sup>48</sup> Genner and Boas,<sup>49</sup> Chambers and Koetter,<sup>50</sup> Epstein<sup>51</sup> and Epstein and Chambers.<sup>52</sup>

According to the present consensus, the nonkeratotic gonorrheal exanthemas do not constitute separate entities. Erythemas, urticarias, erythema-multiforme-like or erythema-nodosum-like, as well as hemorrhagic-bullous lesions, are found simultaneously or successively in many cases, and they are to be considered as different evolutionary

43 Stanislawski, W. Ueber einen Fall von gonorrhoeischer Urethritis mit Affektion der Gelenke, symmetrischem hornartigen Hautausschlag und Ausfallen der Nagel, Monatsb d Krankh d Harn- u Sex-Appar **5** 643, 1900

44 Frei, W. Gonorrhoeisches Exanthem und Enanthem bei Arthritis gonorrhoeica, Zentralbl f Haut- u Geschlechtskr **4** 323, 1922

45 Barrett, C. C. Keratosis Blennorrhagica, Arch Dermat & Syph **22** 627 (Oct) 1930

46 Guerrieri, T. Blenoderma cheractosico, Giorn ital d mal ven **65** 361, 1924

47 Bogrow, S. L. Ueber gonorrhoeische Keratosen. Ein Fall von gonorrhoeischen Keratosen der Haut und Mundschleimhaut, Arch f Dermat u Syph **143** 23, 1923

48 Berman, L. Ueber einen Fall von gonorrhoeischer Keratose der Haut und Mundschleimhaut, Dermat Ztschr **51** 420, 1928

49 Genner, V., and Boas, H. Case of Gonorrheal Blennorrhagicum, Arch Dermat & Syph **9** 423 (April) 1924

50 Chambers, S. O., and Koetter, G. F. Keratosis Blennorrhagica, Arch Dermat & Syph **27** 411 (March) 1933

51 Epstein, E. Hyperpyrexia in the Treatment of Keratoderma Blennorrhagicum, Am J Syph, Gonor & Ven Dis **21** 148, 1937

52 Epstein, E., and Chambers, S. O. Keratosis Blennorrhagica with Corneal Lesions, Arch Dermat. & Syph **36** 1044 (Nov) 1937



stages of keratosis blennorrhagica, although actual crusting may not be present (Buschke,<sup>53</sup> Buschke and Langer,<sup>54</sup> Hodara,<sup>55</sup> Combes, Dietrich and Cohen<sup>28</sup> and others)

Involvement of the eyes is not infrequently associated with keratosis blennorrhagica, usually as an endogenous and bilateral conjunctivitis which produces a seropurulent, sterile discharge and has a rapid, benign course. Corneal ulcerations (Epstein and Chambers<sup>52</sup>) as well as anterior synechias, iridocyclitis and retinitis have rarely been reported. Other rare complications may be acute glomerular nephritis (Spink and Keefer<sup>56</sup>), hepatitis with hypochromic anemia, general lymphadenopathy, tenosynovitis and buisitis. Endocarditis was rarely observed in this disease (Neiders,<sup>57</sup> Reiss,<sup>58</sup> Sullivan<sup>35</sup> and Welander<sup>59</sup>) and myocarditis was reported only in 1 case to our knowledge (Gadrat and Morel<sup>41</sup>)

The general condition of the patient is usually grave. The temperature is swinging, with daily peaks of between 100 and 102 F for several weeks. The mental condition of the patient is poor, bordering on melancholia and often on lethargy. Some authors have suggested that this condition is due to the effect of gonococci and their toxins on the cord and the higher centers (Jeanselme,<sup>60</sup> Launois,<sup>61</sup> Jacquet and Ghika<sup>62</sup> and Buschke<sup>53</sup>). However, neurologic examinations do not as a rule reveal any essential changes or abnormalities.

The course of the disease is slow, exacerbations of symptoms referable to joints, eyes and skin are frequent long after the urethritis has cleared. The patient loses weight rapidly and becomes debilitated.

53 Buschke, A. Ueber universell symmetrische entzündliche Hyperkeratosen auf uro-septischer und arthritischer Basis, *Arch f Dermat u Syph* **113** 223, 1912

54 Buschke, A., and Langer, E. Hyperkeratotische Exantheme bei Gonorrhoe und ihre Beziehungen zur Psoriasis, *Dermat Wchnschr* **76** 145, 1923

55 Hodara, A. Ein Fall von Gonokokämie und generalisiertem gonorrhöischem Exanthem, *Dermat Wchnschr* **55** 397, 1912

56 Spink, W. W., and Keefer, C. S. Renal and Dermatologic Complications of Gonococcus Infections, *New England J Med* **217** 241, 1937

57 Neiders, K. Ein Fall von Keratosis gonorrhoeica, *Dermat Wchnschr* **1** 751, 1934

58 Reiss, Gonorrhöische Sepsis, *Zentralbl f Haut- u Geschlechtskr* **37** 580, 1931

59 Welander, E. Ein Fall von Blennorrhoe, mit Endocarditis und kutanen Manifestationen kompliziert, *Monatsh f prakt Dermat* **21** 50, 1895

60 Jeanselme, E. Troubles trophiques dans la blennorrhagie, *Ann de dermat et syph* **6** 525, 1895

61 Launois, P. E. Arthropathies recidivantes, amyotrophie generalisee, troubles trophiques multiples d'origine blennorrhagique, *Bull et mem Soc med d hop de Paris* **16** 736, 1899

62 Jacquet, L., and Ghika. Sur un cas d'arthro-blennorrhagisme avec troubles trophiques, *Bull et mem Soc med d hôp de Paris* **14** 93, 1897

and cachectic, the muscles around the involved joints waste away rapidly. After a course of several months the arthropathies clear up as a rule without leaving any permanent damage, although a few cases of anklyosis have been reported. The involution of the cutaneous lesions is extremely slow, but they heal without leaving any scars. Relapses are not infrequent and are commonly associated with recurrences of gonorrheal adnexal inflammations or reinfections. Death due to intercurrent diseases and cachexia has been reported in about 10 per cent of the cases (Sutton and Sutton<sup>63</sup>).

#### HISTOPATHOLOGY

The histologic characteristics of keratosis blennorrhagica were studied by Chauffard and Fiessinger,<sup>23</sup> Arning and Meyer-Delius,<sup>4</sup> Buschke and Michael,<sup>64</sup> Baermann,<sup>37</sup> Paschen and Jentz,<sup>65</sup> Haase,<sup>66</sup> Langer,<sup>2</sup> Sobotka,<sup>67</sup> and Adamson,<sup>68</sup> and were described in great detail by Keim,<sup>69</sup> Gans,<sup>70</sup> Simpson<sup>22</sup> and Rostenberg and Silver.<sup>71</sup>

The histologic picture is not sharply specialized, it shows similarities with other types of exanthemas, and it varies according to the age and site of the lesions. The earliest manifestation is an exudatory, inflammatory process in the prickle cell layer of the epithelium and papillary and subpapillary layers of the corium. There is vesicle formation in the rete, the contents of these vesicles soon showing polymorphonuclear neutrophils, leukocytes and plasma cells. There is an intracellular and intercellular edema. The tops of the vesicles are formed by one or two layers of squamous cells and a thinning stratum corneum. The base of the vesicle is formed by an increasingly acanthotic, edematous rete. After the vesicle becomes a pustule it breaks open, forming hard, thick parakeratotic crusts. An increased number of mitotic cells

63 Sutton, R. L., and Sutton, R. L., Jr. *Diseases of the Skin*. St. Louis, C. V. Mosby Company, 1939, p. 969.

64 Buschke, A., and Michael, S. Zur Kenntnis der hyperkeratotisch-vesikulösen Exantheme bei Gonorrhoe, *Arch. f. Dermat. u. Syph.* **120** 348, 1914.

65 Paschen, E., and Jentz, E. Ein Beitrag zur Frage der spezifischen Ätiologie gonorrhöischer Exantheme, *Med. Klin.* **1** 428, 1922.

66 Haase, M. Keratosis Blennorrhagica, *J. Cutan. Dis.* **34** 817, 1916.

67 Sobotka. Pustulos-hyperkeratotisches Exanthem bei gonorrhöischer Allgemeinerkrankung, *Dermat. Wchnschr.* **56** 181, 1913.

68 Adamson, H. G. Keratoderma Blennorrhagica. Is It a Form of Psoriasis? *Brit. J. Dermat.* **32** 183, 1920.

69 Keim, H. L. The Histogenesis of Keratoderma Blennorrhagicum, *Arch. Dermat. & Syph.* **9** 423 (April) 1924.

70 Gans, O. *Histologie der Hautkrankheiten*, Berlin, Julius Springer, 1925, vol. 1, p. 348.

71 Rostenberg, A., and Silver, H. Keratoderma Blennorrhagicum, *Arch. Dermat. & Syph.* **16** 741 (Dec.) 1927.

can be observed in the squamous layer and over it a parakeratotic stratum corneum of varying thickness, indicating acceleration of the proliferative processes leading to incomplete keratinization (parakeratosis). In the papillary and subpapillary layers there is perivascular infiltration with leukocytes, polymorphonuclears and plasma cells surrounding the distended vessels and the follicles.

#### PATHOGENESIS

The cause of keratosis blennorrhagica has been the subject of much discussion, especially since Adamson<sup>68</sup> in 1920 and several other authors raised the question of its close relation to arthropathic psoriasis. Its gonorrheal origin has been doubted, denied and confirmed repeatedly. Recently its relation to Reiter's disease emerged as a new point of discussion. Since Wiedmann<sup>72</sup> in 1934 reported the first case of Reiter's syndrome with keratosis several other authors have reported cases with similar interpretations. Kuske<sup>73</sup> even suggested that keratosis blennorrhagica is always due to Reiter's syndrome. Other authors, considering the lack of evidence as to a gonorrheal infection in several reports, doubted the specific gonorrheal character of the disease and, although they admitted a possible gonorrheal causation, expressed the opinion that other causes may also be responsible (Buschke,<sup>74</sup> Langer,<sup>2</sup> Gottron,<sup>75</sup> Loefgren,<sup>76</sup> Mastrojanni,<sup>3</sup> Baermann,<sup>37</sup> Pawlow and Schindelkroitt,<sup>77</sup> Gadrat,<sup>78</sup> Genner and Boas,<sup>49</sup> Scholtz,<sup>20</sup> Silver<sup>79</sup> and Eisner<sup>80</sup>).

Thus one has the opinions of three groups: (1) those denying a gonorrheal causation, (2) those doubting the specific nature of the disease, calling it a syndrome with various causes but with common clinical and pathologic features and (3) those accepting gonorrheal infection as the only primary etiologic factor but (a) believing in

72 Wiedmann: Reitersche Erkrankung, *Wien klin Wchnschr* **47** 1245, 1934.

73 Kuske, H.: Ueber die Hauterscheinungen bei Morbus Reiter, *Arch f Dermat u Syph* **179** 58, 1939.

74 Buschke, A.: Ueber die sog "Gonorrhoeischen Hyperkeratosen" ohne Gonorrhoe, *Klin Wchnschr* **7** 1133, 1928.

75 Gottron: Gonorrhoeische Sepsis mit Hautexanthem, *Zentralbl f Haut- u Geschlechtskr* **59** 2, 1938.

76 Loefgren, S.: Ein Fall von rezidivierender Keratoderma arthritica, *Acta dermat-venereol* **21** 489, 1940.

77 Pawlow, S., and Schindelkroitt, B.: About the So-Called Gonorrheal Keratodermas, *Sovet vestnik venerol i dermat* **41** 359, 1935.

78 Gadrat, J.: Keratose symetrique et polyarthrite soi-disant blennorrhagique hors de tout gonococcie, *Ann de dermat et syph* **4** 1040, 1933.

79 Silver, H., in discussion on Feldman<sup>66</sup>.

80 Eisner: Hyperkeratosis (Gonorrhoeica?), *Zentralbl f Haut- u Geschlechtskr* **22** 604, 1927.

different pathogenic mechanisms, or (b) believing in other accessory and predisposing causes in addition to gonorrheal infection

The various etiologic interpretations of keratosis blennorrhagica are shown in the outline, which presents the numerous theories concerning the causes of keratosis blennorrhagica and lists the author or authors of each theory

#### I Nongonorrheal causes

- A Disease without gonorrheal exanthema (Balog<sup>81</sup>)
- B Syphilis (Vidal<sup>19</sup>)
- C Reflex manifestation caused by intraurethral manipulation (Finger<sup>82</sup> and Lewin<sup>83</sup>)
- D Secondary organisms or their toxins (Pawlow and Schindelkroitt<sup>77</sup>)
- E Toxic
  - 1 arsphenamine
  - 2 arsenic
  - 3 bromine
  - 4 lead (Thibierge and Weissenbach<sup>82</sup>)
- F Identical with or closely related to arthropathic pustular psoriasis (Adamson,<sup>68</sup> Jadassohn,<sup>38</sup> Waelsch,<sup>83</sup> Falk,<sup>84</sup> Bogrow,<sup>47</sup> Strandberg and Hedenius,<sup>85</sup> Feldman<sup>86</sup> and Silver<sup>79</sup>)
- G Reiter's disease (Kuske<sup>73</sup>)

#### II A nonspecific syndrome (may be gonorrheal or nongonorrheal, other causes besides gonorrhea to which it may be due)

- A Secondary infectious foci or toxins (Strandberg and Hedenius<sup>85</sup> and Pawlow and Schindelkroitt<sup>77</sup>)
- B Nongonorrheal foci of infection or toxins (Pawlow and Schindelkroitt,<sup>77</sup> Buschke and Langer<sup>13</sup> and Jadassohn<sup>38</sup>)
- C Keratotic diathesis as common factor, with different bacterial or toxic causes (Jadassohn,<sup>38</sup> Adamson,<sup>68</sup> Waelsch,<sup>83</sup> Feldman,<sup>86</sup> Buschke<sup>74</sup> and Langer<sup>2</sup>)

81 Balog, cited by Langer,<sup>2</sup> p 67

82 Thibierge and Weissenbach, cited by Scmazzone<sup>7</sup>

83 Waelsch, L Ueber die Beziehungen zwischen Psoriasis und Gelenkserkrankungen, Arch f Dermat u Syph **104** 195 and 453, 1910

84 Falk, A Psoriasis arthropathica (einschliesslich der sog "hyperkeratosen Exantheme" bei gonorrhoeischen Gelenkerkrankungen), Arch f Dermat u Syph **129** 299, 1921

85 Strandberg, J, and Hedenius, J Gonorrheal Keratoderma, Wien Arch f inn Med **51** 6, 1919 Strandberg, J May Keratoderma Appearing in Connection with Joint Affections of Gonorrhoeic or Non-Gonorrhoeic Origin Be Regarded as Expression of Parakeratotic Diathesis? Acta dermat venereol **11**:70, 1930

86 Feldman, S Keratoderma Blennorrhagicum, Arch Dermat & Syph **27** 889 (May) 1933

- D Arthropathy, specific or nonspecific, with disposition for keratosis, which may be
  - 1 familial
  - 2 endocrine
  - 3 metabolic (Lojander<sup>87</sup> and Lohe and Rosenfeld<sup>88</sup>)
- E Nonspecific
  - 1 toxic
  - 2 metastatic
  - 3 septic (Rostenberg and Silver<sup>71</sup>)
- F Reiter's disease (Wiedmann,<sup>72</sup> Kuske,<sup>73</sup> Kruspe,<sup>89</sup> Beck,<sup>90</sup> Postma<sup>91</sup> and Bauer and Engleman<sup>92</sup>)

### III Caused by gonorrheal infection

#### A Direct causes

- 1 Lesions arising as the direct effect of gonorrheal organisms *in loco* (Gougerot and Meaux Saint-Marc,<sup>93</sup> Chauffard and Fiessinger,<sup>28</sup> Kiene,<sup>94</sup> Bogrow,<sup>47</sup> Strominger,<sup>95</sup> Simpson and Beeson,<sup>96</sup> Sullivan, Rolnick and White,<sup>97</sup> Lees and Percival,<sup>24</sup> Szathmary<sup>98</sup> and Aust<sup>99</sup>)

87 Lojander, W    Ueber Keratodermien im Anschluss an Gelenkaffektionen gonorrhoischen und nichtgonorrhoischen Ursprungs, *Acta dermat-venereol* **8** 227, 1927, Ein Fall von Keratoderma arthritica ohne nachweisbare gonorrhoische Infektion, *ibid* **9** 142, 1928

88 Lohe, H, and Rosenfeld, H    Klinische und physiologisch-chemische Untersuchungen über die Hyperkeratosenbildung bei Gonorrhoe und bei Psoriasis pustulosa arthropathica, *Dermat Ztschr* **55** 355, 1929

89 Kruspe    Zur Aetiologie der Reiterschen Erkrankung, *Dermat Wchnschr* **112** 457, 1941

90 Beck, F    Ein Beitrag zur der sog Spirochaetosis arthritica Reiter, *Med Klin* **33** 1162, 1937

91 Postma, C    A Case of Reiter's Disease, *Acta dermat-venereol* **18** 691, 1937

92 Bauer, W, and Engleman, E P    A Syndrome of Unknown Etiology Characterized by Urethritis, Conjunctivitis and Arthritis (So-Called Reiter's Disease), *Tr A Am Physicians* **57** 307, 1942

93 Gougerot and Meaux Saint-Marc    Keratose blennorrhagique disseminee, *guerison, Ann d mal ven* **7** 818, 1912    Gougerot, H, Carteaud, A, and Tardieu, A    Les chancres blennorrhagique, *Arch de dermat Hop St Louis* **1** 201, 1929

94 Kiene, E    Ueber die Pathogenese gonorrhoischer Komplikationen, *Arch f Dermat u Syph* **156** 663, 1928

95 Strominger, L    Quelques considerations sur la keratose blennorrhagique, *J d'urol* **31** 251, 1931, Sur les exanthemes gonococciques, *Rev rom urol* **3** 504, 1936

96 Simpson, F E, and Beeson, B B    Keratoderme Blennorrhagique, *J A M A* **68** 1169 (April 21) 1917

97 Sullivan, S J, Rolnick, H C, and White, C J    Gonorrheal Keratosis Case Report with Experimental Studies, *Illinois M J* **59** 45, 1931

98 Szathmary, S    Beitrage zum Krankheitsbild der Keratosis gonorrhoica, *Orvosi hetil* **2** 905, 1928

99 Aust    Kokkenbefund bei metastatisch-gonorrhoischer Bindehauterkrankung, *Ztschr f Augenh* **65** 299, 1928

- 2 Capillary emboli (Dainow,<sup>100</sup> Photomios and Relias,<sup>101</sup> Bruusgaard and Thjotta,<sup>102</sup> Szathmary<sup>98</sup> and Aust<sup>99</sup>)
- 3 Cocci being destroyed in capillaries, and toxins causing lesions *in loco* (Jadassohn<sup>103</sup>)
- 4 Cocci and their toxins *in loco* together with generalized infection (McDowell<sup>104</sup>)
- 5 Bacteremia, cocci and their toxins in circulation (Buschke and Langer,<sup>1</sup> Jeanselme,<sup>60</sup> Scholtz,<sup>29</sup> Tommasi,<sup>105</sup> Epstein<sup>106</sup> and Thompson<sup>107</sup>)
- 6 Gonorrheal toxemia from gonorrheal foci in glands (Epstein,<sup>106</sup> Scholtz,<sup>29</sup> Haase<sup>66</sup> and Scmazzone<sup>7</sup>)
- 7 Nervous disturbances (Buschke<sup>74</sup>)
- 8 Trophic disturbances, cocci or toxins causing spinal cord disturbances (Jeanselme,<sup>60</sup> Launois,<sup>61</sup> Jacquet and Ghika,<sup>62</sup> Chauffard and Fiesinger<sup>23</sup> and Lees and Percival<sup>24</sup>)
- 9 Allergy to cocci or to their toxins (Garcia,<sup>108</sup> Scmazzone,<sup>7</sup> Sherman, Blumenthal and Heidenreich,<sup>40</sup> Tommasi,<sup>105</sup> Rajam and Rangiah,<sup>27</sup> Combes, Dietrich and Cohen,<sup>26</sup> Lees and Percival,<sup>24</sup> Beeson and Ebert<sup>109</sup> and Ohashi<sup>110</sup>)

B Predisposing and accessory causes

- 1 Secondary infections (Strandberg and Hedenius<sup>85</sup>)
- 2 Idiosyncrasy with keratotic disposition (Photomios and Relias<sup>101</sup>)
- 3 Individual vessel changes (Buschke<sup>74</sup> and DuBois<sup>111</sup>)

100 Dainow, I Contribution a l'etude des métastases cutanees de la blennorragie, Inaug Dissert, Geneva, 1927

101 Photomios, G, and Relias, A Keratodermie blennorrhagique Reproduction experimentale des lésions kératodermiques, Bull Soc franç de dermat et syph **44** 1775, 1937

102 Bruusgaard, E, and Thjotta A Case of Meningitis and Purpura Gonorrhoica, Acta dermat-venereol **6** 262, 1925

103 Jadassohn, J Ueber die Komplikationen der Blennorrhoe, Berlin, Urban & Schwarzenberg, 1906

104 McDowell, J E Keratosis Blennorrhagica or Gonorrheal Keratosis, New York M J **115** 518, 1922

105 Tommasi, L Personal communication to the authors, January 1945

106 Epstein, E Pathogenesis of Keratosis Blennorrhagica, Brit J Dermat **51** 428, 1939

107 Thompson, D O B E Gonorrhea, London, Oxford University Press, 1923, p 231

108 Garcia, F M Keratodermia Due to Gonorrhea, Prensa med argent **20** 739, 1925

109 Beeson, B B, and Ebert, M H Keratodermia Blennorrhagica, Arch Dermat & Syph **31**:740 (May) 1935

110 Ohashi, K Keratosis Blennorrhagica, Jap J Dermat **33** 169, 1933

111 DuBois, C Keratoses blennorrhagiques ou dermatitis gonococciques, Acta dermat-venereol **5** 1, 1924, cited by Gans<sup>70</sup>

- 4 Keratotic disposition    parakeratotic diathesis
  - a Congenital
  - b Acquired
    - (1) Nervous
    - (2) Vegetative
    - (3) Endocrine (Lojander,<sup>87</sup> Strandberg and Hedenius<sup>88</sup> and Lidstrom<sup>112</sup>)
- 5 Associated keratotic and arthropathic disposition (Lidstrom<sup>112</sup> and Buschke and Langer<sup>1</sup>)
  - a On tuberculous basis (Tommasi<sup>105</sup>)
  - b Ether-sulfuric acid increase in joints and skin (Lohe and Rosenfeld<sup>88</sup>)
  - c Vitamin A deficiency (Combes and Behrman<sup>113</sup>)
- 6 Mechanical causes
  - a Inhibition of motion, rest in bed
  - b Increased perspiration, lack of bathing
  - c Compresses, Bier bands (Chauffard and Fiessinger,<sup>23</sup> Buschke<sup>1</sup> and Langer<sup>2</sup>)
  - d Injections of vaccine (Olivet<sup>114</sup>)
- 7 Other dermatoses, pyodermic, follicular lesions (Giessing<sup>115</sup>)
- 8 Roentgen irradiations (Oeltze<sup>116</sup>)

A definitely nongonorrheal etiologic interpretation could never stand up against the overwhelming contrary evidence. The majority of the authors have accepted the specific gonorrheal pathogenesis, while a smaller group have maintained that in some cases a typical picture of keratosis blennorrhagica may develop with a gonorrheal infection. The main points of controversy are therefore formulated as follows:

*I Is keratosis blennorrhagica a specific entity or is it a syndrome with different causes?*

There have been 166 cases reported in the literature in which gonorrhea as the primary cause was not doubted, and only about 34 case reports are known in which the authors did not find any evidence of gonorrheal infection. This ratio is strong evidence in favor of a specific causation.

112 Lidstrom, F. A Contribution to the Question of the Pathogenesis of Gonorrhoeic Keratoderma, *Acta dermat-venereol* **10** 457, 1929.

113 Combes, F. C., and Behrman, H. T. Use of Vitamin A in Keratosis Blennorrhagica, *Arch Dermat & Syph* **46** 728 (Nov) 1942.

114 Olivet, J. Hyperkeratose und Thrombophlebitis bei Gonorrhoe, *Med Klin* **24** 1, 1926.

115 Giessing, H. C. Keratosis Blennorrhagica, *Norsk mag f lægevidensk* **2** 97, 1927.

116 Oeltze, F. W. Ueber Keratosis Gonorrhoeica, *Arch f Dermat u Syph* **144** 1, 1923.

Baermann gave the following argument in favor of a specific character of the disease (a) It is constantly associated with gonorrhea The cutaneous eruption waxes and wanes with the exacerbations and remissions of the gonorrheal infection (b) No similar eruption is found in any other disease or as an idiopathic disease

In the light of the newer conception of gonorrheal latency some cases reported as nongonorrheal may leave considerable doubt as to their real nonspecific nature In spite of the failure to observe gonococci the history of previous gonorrheal infections, the presence of urethritis, prostatitis, vesiculitis, arthritis and, often, metastatic conjunctivitis should be strongly suggestive of a latent gonorrheal focus

Langer analyzed the case reports of Launois,<sup>61</sup> Baermann,<sup>37</sup> Malherbe,<sup>34</sup> Bogrow,<sup>47</sup> Scholtz<sup>20</sup> and Jones<sup>28</sup> with the aforementioned conclusion However, he as well as Buschke saw patients with typical keratosis but without any evidence of gonorrhea and modified their conception, after much hesitation, in favor of a possible, though rare, nonspecific cause Langer<sup>2</sup> also pointed out that the patients of Buschke and Langer,<sup>117</sup> Lojander,<sup>87</sup> Lohe and Rosenfeld,<sup>88</sup> Rostenberg and Silver<sup>71</sup> and Eisner<sup>80</sup> had prostatitis and vesiculitis associated with their urethral discharge and showed all the characteristics of gonorrheal keratosis except that gonococci were not observed

The fact that in some of these cases the disease resembled pustular arthropathic psoriasis made some authors believe in the possibility of a common cause of the two diseases (Adamson,<sup>68</sup> Michael,<sup>118</sup> Lojander,<sup>87</sup> Lohe and Rosenfeld,<sup>88</sup> Buschke and Langer,<sup>117</sup> Flynn,<sup>119</sup> Mitchell,<sup>120</sup> Waelsch<sup>83</sup> and Falk<sup>64</sup>) and for a while the main point of discussion was stated as follows

## *II What is the relation of keratosis blennorrhagica to arthropathic psoriasis?*

The question was answered by Keim's<sup>69</sup> excellent work on the pathology of the two diseases He demonstrated clearly that they are two different entities and his observations were corroborated by other authors (Gans,<sup>70</sup> Haase<sup>66</sup> and Rostenberg and Silver<sup>71</sup>)

Apart from the differences in the general systemic picture and clinical course, the two diseases have also decided histologic differences Psoriatic lesions do not begin as vesicles, and plasma cells are not seen in the infiltration

117 Buschke, A, and Langer, E. Hyperkeratotische Exantheme bei Gonorrhoe und ihre Beziehungen zur Psoriasis, *Dermat. Wchnschr* 76.145, 1923

118 Michael, M. Urethritis non gonorrhoeica, Arthritis pseudogonorrhoeica, *Dermat. Ztschr* 24:419, 1917

119 Flynn, J W. Keratoderma Blennorrhagicum, *M J Australia* 2 680, 1927

120 Mitchell. Blennorrhagic Keratoses, Arthritis, Psoriasis, *Arch Dermat & Syph* 18:979 (Dec) 1928



Epstein<sup>121</sup> listed the differential diagnostic points between keratosis blennorrhagica and psoriasis as follows

(a) In keratosis blennorrhagica the crusts are firmly attached and are hard to remove

(b) There are no bleeding points after removal of crusts in keratosis blennorrhagica

(c) The lesions begin as vesicles, a process not seen in psoriasis

(d) Arthritis precedes the exanthema, while in psoriasis arthritis is a late symptom

(e) Typical localization of cutaneous lesions on the feet, on the soles and only rarely on the elbows occurs in keratosis blennorrhagica

(f) Large joints are involved chiefly in keratosis blennorrhagica, the arthritis causes no deformities, its onset is acute, and it clears rapidly. In psoriasis the small joints, fingers and toes are involved chiefly, the course is extremely chronic, and deformities are common

(g) Gonorrheal keratosis is associated with a graver general condition

(h) There are differences in the lesions of the mucous membrane and the involvement of the nails

(i) Fever therapy is not successful in the treatment of psoriasis

Undoubtedly, there are certain morphologic similarities between the two diseases, but according to the present consensus there does not seem to be a deeper connection, and they should be considered as two separate entities

More recently, cases in which this question might be discussed have been reported only rarely (Feldman<sup>86</sup>). However, in the last ten years a new point of discussion was brought into the literature by European authors, the relation of keratosis blennorrhagica to Reiter's disease

### *III What is the relation of keratosis blennorrhagica to Reiter's disease?*

Wiedmann in 1934 was the first to interpret his case of keratosis as a case of Reiter's disease. Up to the present time, 13 cases of keratosis have been reported with a similar interpretation in 10 communications by the following authors: Wiedmann,<sup>72</sup> Naegeli,<sup>122</sup> Kuske,<sup>73</sup> Kruspe,<sup>89</sup> Beck,<sup>90</sup> Postma,<sup>91</sup> Bauer and Engleman<sup>92</sup> and Lever and Crawford<sup>123</sup>

Reiter's disease, which was first reported by Reiter<sup>124</sup> in 1916 as a spirochetal infection, is actually a syndrome of urethritis, conjunctivitis and arthritis in which gonococci or micro-organisms cannot be demon-

121 Epstein, E. Differential Diagnosis of Keratosis Blennorrhagica and Psoriasis Arthropathica, *Arch Dermat & Syph* **40** 547 (Oct) 1930

122 Naegeli, O. Morbus Reiter mit Hautexanthem, *Schweiz med Wchnschr* **67** 63, 1937, **68** 793, 1938

123 Lever, W. F., and Crawford, G. M. Keratosis Blennorrhagica Without Gonorrhea (Reiter's Disease?), *Arch Dermat & Syph* **49** 389 (June) 1944

124 Reiter, H. Ueber eine bisher unbekannte Spirochaeten Infektion (Spirochaetosis arthritica), *Deutsche med Wchnschr* **42** 1529, 1916

strated According to Lever and Crawford,<sup>123</sup> 47 cases were reported in 25 communications, including their own, in 13 of which it was associated with keratotic cutaneous lesions However, the existence of Reiter's disease as an entity has not yet been proved beyond doubt The case reports are somewhat conflicting, in some the bacterial studies did not seem adequate to exclude the presence of a gonorrheal infection and in others the history of the patient and some clinical observations strongly suggested the possibility of a latent gonorrhea (3 cases reported by Kuske,<sup>72</sup> 2 cases by Foerster<sup>125</sup>)

However, there remain about a score of case reports of keratosis blennorrhagica in the literature with sufficient evidence to exclude gonorrhea, a number small enough in comparison with the number of cases with a definitely or suspectedly gonorrheal origin to raise serious doubts about the specific nature of keratosis blennorrhagica While it may not be possible to give a satisfactory explanation of the relation of this small number of cases of nongonorrheal keratosis to the number of cases of gonorrheal keratosis, either by assuming that they are due to an undemonstrable latent gonorrheal focus or by classifying them as psoriasis, we can safely conclude that the majority of evidence as well as the majority of authors favor a specific gonorrheal causation of keratosis blennorrhagica

In the majority of cases the complement fixation test for gonorrhea elicited a positive reaction However, owing to the numerous negative results in cases of evidently gonorrheal keratosis and to the occasional reports of false positive reactions, the reliability of this test has been questionable, and it has not been used by many authors

Even though gonorrheal infection is accepted as the specific cause, the actual pathogenesis of the disease is interpreted differently, leading to some controversy among the authors The main point of discussion can be formulated as follows

*IV Are the cutaneous, synovial and conjunctival affections of keratosis blennorrhagica caused by the presence of the Neisserian organisms in loco, or by toxic, allergic, trophic or other factors?*

The advocates of the "direct effect" conception offer mainly the argument that the gonococci have been demonstrated in the lesions in some patients and that, if their toxins are responsible, the cocci must be present *in loco* because they liberate their endotoxins only while in the process of disintegration

Contrary to this, the toxic-allergic interpretation holds that the gonococci, because of their biologic properties, cannot vegetate in the skin

125 Foerster, R Zwei Faelle von Reiterscher Erkrankung, Med Welt 7: 700, 1933

and are also quickly destroyed in the blood. Furthermore, the organisms have been demonstrated in the lesions as well as in the blood only on rare occasions.

The number of case reports of positive evidence of gonococci in the cutaneous lesions of keratosis blennorrhagica collected from the literature by most authors has numbered less than a half dozen. Careful search of the literature, however, yields a much higher number.<sup>126</sup> To obtain complete bacteriologic data on the disease, we have collected the instances of gonococci in the blood,<sup>127</sup> joints<sup>128</sup> and conjunctivas<sup>129</sup> in all types of gonorrheal exanthemas, as shown in tables 2 and 3.

While not all the positive observations of gonococci are entirely convincing in the reports of the authors listed in tables 2 and 3, the majority of them must be considered reliable. For instance, Roark<sup>127b</sup> was not convinced that his blood culture contained typical gonococci.

126 (a) Bulkin, A. Ein Fall von Keratosis blennorrhagica, *Vestnik dermat.* **5** 2, 1927. (b) Gager, E. C. Keratoderma Blennorrhagica, *J. A. M. A.* **78** 941 (April 1) 1922. (c) Wadsack, E. Ein gonorrhoeisches Exanthem, *Berl. klin. Wchnschr.* **43** 966, 1906. (d) Campbell, J. R., cited by Sutton, R. L. *Diseases of the Skin*, ed. 5, St. Louis, C. V. Mosby Company, 1923, p. 438. (e) Barrett, C. C. Keratoderma Blennorrhagicum, *Arch. Dermat. & Syph.* **22** 627 (Oct.) 1930. (f) Fuhs. Acrodermatitis continua mit chronischer deformierender Polyarthritits, *Zentralbl. f. f. Haut- u. Geschlechtskr.* **63** 409, 1940. (g) Portugal, H., Cunha, and Machado. Ceratoderma blennorrhagica, *Ann. brasil. de dermat.* **13** 55, 1938. (h) Cole, H. N., and Driver, J. R. Keratoderma Blennorrhagica, *Arch. Dermat. & Syph.* **19** 1025 (June) 1929. (i) Hansteen, E. H. Keratosis Gonorrhoeica, *Internat. Clin.* **4** 62, 1927. Dubois<sup>111</sup> Dainow<sup>100</sup> Photonios and Relias<sup>101</sup> Strominger<sup>95</sup> Combes and Behrman<sup>113</sup> Scholtz<sup>29</sup> Szathmary<sup>98</sup>.

127 (a) Jenkins, J. A. Gonococcal Septicaemia, *Brit. M. J.* **1** 641, 1922. (b) Roark, B. H. Blennorrhagic Keratosis, *J. A. M. A.* **59** 2039 (Dec. 7) 1912. (c) Massini. Ueber gonorrhoeische Sepsis, *Ztschr. f. klin. Med.* **83** 1, 1918. (d) O'Brien, T. J., and Bancker, E. Gonococcus Sepsis, *New England J. Med.* **198** 184, 1928. (e) Hazel, O. G., and Snow, W. B. Gonococcic Septicemia with Purpura and Arthritis Successfully Treated by Hyperthermia, *J. A. M. A.* **109** 1275 (Oct. 16) 1937. (f) Kerl. Gonokokkenexantheme, *Zentralbl. f. Haut- u. Geschlechtskr.* **49** 587, 1934. (g) Friedberg, C. K. Gonococcemia with Recovery, *Am. J. M. Sc.* **188** 271, 1934. (h) Wiedmann, A. Beitrage zur Pathologie der Gefasserkrankungen der Haut, *Dermat. Wchnschr.* **98** 541, 1934. (i) Wheeler, G. W., and Cornell, N. W. Gonorrheal Bacteremia in a Woman, with Apparent Cure by Surgical Intervention, *J. A. M. A.* **94** 1568 (May 17) 1930. (j) Chevalier, P., Levy-Bruehl, and Bourgeois. Purpura generalise chronique et presque apyretique d'origine gonococcique, *Bull. et mem. Soc. med. d. hôp. de Paris* **1** 30, 1927. Hodara<sup>55</sup> Chauffard and Fieissinger<sup>23</sup> Dainow<sup>100</sup> Bruusgaard and Thjotta<sup>102</sup>.

128 (a) Bejarano, J., and Orbaneja, J. G. Contribution a l'étude des syndromes cutanes articulaires, *Ann. de dermat. et syph.* **6** 994, 1935. (b) Jobst. Arthritis Gonorrhoeica, *Gyogyaszat* **68** 365, 1928. Fuhs<sup>126</sup> Strominger<sup>95</sup>.

129 Stewart, W. M. A propos d'un cas de keratose gonococcique, *Bull. Soc. franç. de dermat. et syph.* **47** 160, 1940. Aust<sup>99</sup>.

Portugal, Cunha and Machado <sup>120g</sup> gave no details of the methods and circumstances by which "occasional gonococci" were demonstrated in the cutaneous lesions. On the other hand, in Hodara's case, <sup>55</sup> the positive evidence was obtained from erythematous lesions which later became keratotic.

TABLE 2—*Positive Evidence of Gonococci in Typical Cases of Keratosis Blennorrhagica*

Skin	By culture or smear	Bulkin <sup>126a</sup> , Gager <sup>126b</sup> , Wadsack <sup>126c</sup> , Campbell <sup>126d</sup> , Barrett <sup>126e</sup> , DuBois <sup>111</sup> , Dainow <sup>100</sup> , Fuhs <sup>126f</sup> , Portugal, Cunha and Machado <sup>120g</sup> , Photonios and Rellas <sup>101</sup> , Strominger <sup>95</sup> , Cole and Driver <sup>126h</sup> , Combes and Behrman <sup>113</sup> , Hansteen <sup>126i</sup> , Scholtz <sup>29</sup>
	By histologic examination	Szathmary <sup>98</sup> , Bulkin <sup>126a</sup>
Joints	By culture or smear	Fuhs <sup>126f</sup> , Strominger <sup>95</sup> , Bejarano and Orbaneja <sup>128a</sup>
Eye	By smear	Stewart <sup>129</sup>
	By histologic examination	Aust <sup>99</sup> , previous case referred to by Aust <sup>99</sup>
Blood	By culture or smear	Hodara <sup>55</sup> , Chauffard and Flessinger <sup>28</sup> , Jenkins <sup>127a</sup> , Dainow <sup>100</sup> , Roark <sup>127b</sup>

TABLE 3—*Positive Evidence of Gonococcus in Nonkeratotic Gonorrheal Exanthemas*

Skin	By culture or smear	Lohe <sup>130a</sup> (herpetic), Chevallier, Levy-Bruehl and Bourgeois <sup>1271</sup> (purpura), Dorner <sup>130b</sup> (erythema), Siegel <sup>130c</sup> (hemorrhagic pustular), Hodara <sup>55</sup> (erythema), Wolfram <sup>130d</sup> (vesiculopustular), Nitto and Yoshihiro <sup>130e</sup> , Kerl <sup>127f</sup> (pustules), Henning <sup>130f</sup> (vesicles), Pugh <sup>130g</sup> (abscesses)
	By histologic examination	Bruusgaard and Thjotta <sup>102</sup> (in precapillaries of skin and endothelium), Itchikawa and Ohmori <sup>130h</sup> (erythema multiforme like), Paschen and Jentz <sup>95</sup> (hemorrhagic bullous)
Joint*	By culture or smear	Jobst <sup>128b</sup> (in 12 cases)
Blood	By culture or smear	Bruusgaard and Thjotta <sup>102</sup> , Massini <sup>127c</sup> , O'Brien and Bancker <sup>127d</sup> , Hazel and Snow <sup>127e</sup> , Kerl <sup>127f</sup> (2 cases), Friedberg <sup>127g</sup> (3 cases), Wiedmann <sup>127h</sup> , Wheeler and Cornell <sup>127i</sup> (7 cases), Chevallier, Levy Bruehl and Bourgeois <sup>1271</sup>
Liquor spinalis	By smear from spinal fluid in case of gonorrheal septicemia	Decrop, G. Bull Soc franç de dermat et syph 44 461, 1937
Heart	By culture from tricuspid and mitral valves after death	Brunet <sup>121</sup>

Seventeen positive observations of gonococci in 166 case reports amounts to about 10 per cent positive bacterial evidence as to the presence of gonococci in the keratotic cutaneous lesions.

Such a high percentage, never before reported by any other authors, should establish beyond doubt the immediate role of the Neisserian organism in the pathogenesis of gonorrheal keratosis. If we add the

80 case reports of nonkeratotic gonorrheal dermatoses and their 13 positive bacterial showings<sup>130</sup> to the cited figures, the percentage of positive observations of gonococci in all types of gonorrheal lesions of the skin is 12.2 per cent.

In contrast to this relatively high percentage, the cultures of the blood only rarely yield gonococci, not only in typical cases of keratosis blennorrhagica but in cases of all types of systemic gonorrheal infections. Even in the severest gonorrheal septicemias, gonococci can rarely be cultured from the blood, probably because they are killed rapidly by its bactericidal properties. Brunet<sup>131</sup> cultured gonococci from the mitral and tricuspid valves of the heart after death of a patient in whose blood he had not been able to demonstrate them with repeated cultures, in spite of the severe septicemic condition which eventually resulted in the patient's death.

Similarly, in the fluid obtained by puncture of joints in gonorrheal arthritis, bacterial evidence is rarely demonstrated. Jadassohn<sup>103</sup> attributed this to the following reasons: 1. The cocci vegetate only in the synovial membrane and do not get into the cavity. 2. If they reach the cavity they are quickly destroyed by the synovial fluid. 3. They may get into the cavity very early or very late in the course of the disease.

The synovial fluids in which gonococci are found have lower bactericidal properties than the blood, whereas a sterile synovial fluid has the same bactericidal capacity as the blood, according to Spink and Keefer<sup>56</sup>. The gonococci are quickly destroyed in the synovial fluid, and are never found after the sixth day.

Jobst,<sup>128b</sup> who reported 12 positive observations in cases of gonorrheal arthritis, attributed the gonorrheal condition of the joints to a disposition created by precurent tuberculosis, an opinion which is shared by Tommasi<sup>105</sup> and others. Jobst found 5 per cent gonorrheal arthritis.

130 (a) Lohe, H. Ueber einen Fall von herpetiformen, gonorrhaischem Exanthem, *Dermat Ztschr* **15** 475, 1908, Psoriasis pustulosa, *Zentralbl f Haut- u Geschlechtskr* **28** 416, 1929. (b) Dorner, L. Ueber Gonokokkensepsis, *Deutsche med Wchnschr* **49** 1549, 1923. (c) Siegel, L. A. A Case of Gonococcus Septicemia, *Bull Buffalo Gen Hosp* **3** 66, 1925. (d) Wolfram. Vesiculopustuloes-hamorrhagisches Gonokokkenexanthem, *Zentralbl f Haut- u Geschlechtskr* **59** 381, 1938. (e) Nitto, S., and Yoshihiro, I. A Case of Gonorrheal Exanthema, *Jap J Dermat* **41** 111, 1937. (f) Henning, L. Gonorrhaische Hautaffektion beim Saugling, *Dermat Wchnschr* **92** 96, 1931. (g) Pugh, W. S. Skin Complications of Gonorrhea, *Am Med* **36** 126, 1930. (h) Itchikawa, T., and Ohmori, S. Gonococcus Exanthema, *Jap J Dermat* **34** 511, 1933. Chevalier, Levy-Bruehl and Bourgeois<sup>127j</sup>. Kerl<sup>127f</sup>. Hodara<sup>55</sup>. Bruusgaard and Thjotta<sup>102</sup>. Paschen-Jentz<sup>65</sup>.

131 Brunet, W. M. Gonococcal Endocarditis, *Am J Syph* **23** 207, 1939.

instead of the usual 2 per cent among the miners of Pécs, Hungary, where conditions were poor and the rate for tuberculosis was extremely high

In only 1 case of metastatic conjunctivitis could gonococci be demonstrated in the seropurulent discharge of the conjunctiva (Stewart<sup>129</sup>) Aust<sup>99</sup> in 1928 demonstrated gonococci in the biopsy specimen taken from the bulbar conjunctiva of a patient suffering with endogenous conjunctivitis, the second such histologic observation, according to his statement

Further evidence in favor of the "direct effect" conceptions may be seen in the results of the following experiments In keratotic patients of Chauftard and Friessinger<sup>23</sup> and Sullivan, Rolnick and White<sup>97</sup> new keratotic lesions were produced by inoculating intact sites on the skin with the scrapings of old lesions Similar lesions developed on the arms of the patients of Szathmary<sup>98</sup> and Scmazzone<sup>7</sup> after inoculation with pus of a urethral discharge containing gonococci Lees and Percival<sup>24</sup> reported the same results with cultures of gonococci Photonios and Relias<sup>101</sup> not only produced new lesions by inoculating scrapings of old lesions containing gonococci but also could demonstrate the cocci in the reinoculated lesions

In support of the toxic-allergic interpretation, equally strong arguments have been brought forth Epstein<sup>106</sup> listed his reasons for a toxic interpretation as follows (1) rarity of evidence of gonococci in lesions, (2) symmetry of lesions, (3) involvement of mucosae, (4) sterile, toxic conjunctivitis, (5) localization, (6) clearing of lesions with the cure of infectious foci in the adnexa, (7) uselessness of local applications, and (8) coexistence of urethritis and arthritis with the cutaneous lesions

Scholtz<sup>20</sup> reported that injections of gonococcus vaccine caused new showers of cutaneous eruption Olivet<sup>114</sup> noticed that new keratotic lesions developed at the sites of injections of gonococcus vaccine In 1 of their patients, Buschke and Langer<sup>1</sup> observed the reddening and flare-up of lesions after intravenous administrations of gonococcus vaccine Scmazzone<sup>7</sup> and others reported cases in which the onset of keratosis occurred after injections of vaccine in subjects with long histories of gonorrhea

We may add that the general picture of keratosis blennorrhagica is not that of an acute septicemia (Kiene<sup>94</sup>), the arthritis is rarely the phlegmonous, ankylosing variety but is rather a benign seropurulent exudatory type, and the cutaneous lesions are not those of the bacterial-pyodermic dermatoses but resemble more a chronic toxic-allergic process The symmetry, appearance and localization of keratoses on the extremities and the condition of the nails may justly suggest toxic-trophic disturbances, an interpretation of Jeanselme,<sup>60</sup> Jacquet and Ghika<sup>62</sup> and others

Recently the more functional allergic conception has come into the foreground. Proponents of this concept have expressed the belief that the gonococci or their toxins affect the neurovegetative-endocrine balance, causing colloidal disturbances in the cells, a tissular shock leading to sensitization of certain portions of the skin (Garcia<sup>108</sup> and Scomazzoni<sup>7</sup>).

While some aspects of the disease may fit one or the other of these interpretations well, not all the cases nor all of their features can be sufficiently explained by any single "cause." Neither could we obtain a satisfactory explanation by simply adding one cause to another or by the supposition of additional predisposing causes, as a strictly morphologic approach would attempt further clarification.

It is safe to say that one is dealing here with a complex functional disturbance of the whole organism, the magnitude and gravity of which are not in proportion to the extent and duration of the bacterial invasion or of a toxic saturation.

While the physiopathologic allergic interpretation seems to give a broader understanding of this as well as of many other diseases, it is still difficult to explain the total picture of gonorrheal keratosis by the sensitization of only certain portions of the skin, joints and conjunctivas by the cocci or toxins, either directly or through a more general disturbance in the nervous system and the neurovegetative-endocrine systems.

The process, as most authors agree, begins with the invasion of the circulatory system by gonococci, most probably from an adnexal abscess which erodes into the blood stream. The curious fact that chiefly men are affected by keratosis blennorrhagica or by other systemic manifestations of gonorrhea is difficult to understand. This may be explained, perhaps, by the greater likelihood of abscesses forming and breaking into vessels of the interstitium in the male adnexal organs, owing to their anatomic structural properties.

Invasion of the circulatory system by gonococci is not likely to be a rare occurrence if one considers the high incidence (2 per cent) of gonorrheal arthritis and the frequent general symptoms, such as chills and fever, in exacerbations of prostatitis and vesiculitis. It is extremely probable that in many gonorrheal infections such an invasion occurs repeatedly and may well lead to an allergic sensitization, the disintegration products of gonococci acting as allergens. It may be of some significance that in most cases keratosis blennorrhagica develops in the fourth decade, usually after a protracted or a repeated attack of gonorrhea. The pus discharged into the blood stream is carried to the various organs as small emboli, according to Hodara,<sup>55</sup> Massini,<sup>127c</sup> Bruusgaard and Thjotta<sup>102</sup> and others. These emboli contain cocci of different virulence and in various stages of disintegration. Caught in the small precapillaries, these emboli and cocci break down quickly, all evidence

pointing toward the fact that gonococci cannot vegetate in the blood or tissues because of their biologic properties and the gonococcal properties of the blood and tissue fluids (Friedberg,<sup>127g</sup> Wheeler and Cornell,<sup>127i</sup> Kiene,<sup>94</sup> Tommasi<sup>105</sup> and others)

According to the virulence of the cocci and the constitution of the patient, the result of such an invasion may range from slight malaise with no apparent consequences to an acute and grave septicemia associated with endocarditis, arthritis, meningitis and hemorrhagic-bullous, pustular and erythema-nodosum-like cutaneous lesions. For true gonococcal septicemia a mortality of 93 per cent has been reported by Bakst, Foley and Lamb.<sup>132</sup> In gonococcal septicemia allergic manifestations due to previous sensitization may be present although not predominant, however, bacterial-toxic factors stand in the foreground and the course is rapid and severe.

In typical keratosis blennorrhagica the invasion by gonococci may produce pathologic changes in the organism attributable directly to the presence of gonococci *in loco*. This stage does not last long, owing to the rapid disintegration of the invading organism, and it rarely leads to true septicemia (Kiene<sup>94</sup>). The ensuing long illness and the grave general condition of the patient cannot be explained entirely, therefore, by bacterial and toxic causes. The extent and duration of the symptoms are certainly out of proportion to a possible, even if repeated, small scale bacterial infiltration, or to toxic causes originating from the primary focus. The presence of secondary organisms as the cause is highly doubtful, as they have never been demonstrated during the extremely long course of keratosis blennorrhagica. Neither does a piecemeal sensitization of certain tissues and portions of the skin give a plausible explanation for the whole picture of the disease. This picture suggests that we are dealing here primarily not with a skin problem but with a hyper-reactive organism (in the sense of pleoergy of von Groer) sensitized by previous attacks of gonococci to such a degree that the repeated presence, no matter how small, of the gonococci in the system elicits an organismal reaction far beyond that which would be adequate to cope with the actual infection, a quasidesperate reaction in which the organism spends itself and perhaps breaks down completely.

Thus one observes the rapid pulse, the excessive perspiration and the continued swinging temperature without any bacterial evidence to account for these violent reactions. In the skin the reaction is the exudative-vascular type characterized by an acceleration of the proliferative processes and by the heaping up of immense amounts of corneous material and finally resulting in a broken-down erythrodermic skin.

<sup>132</sup> Bakst, H., Foley, J. A., and Lamb, M. Gonorrheal Septicaemia and Erythema Nodosum, *Ann Int Med* 9:970, 1935.

<sup>133</sup> Footnote deleted by the authors.



Furthermore, one can observe the mental attitude of utter defeat, the cachexia and the wasting away of the body without microscopic and serologic examinations revealing sufficient reasons to explain them

A disease implies not only morphologic tissular change and damage caused directly by the pathogenic agent but also a functional readjustment of the total organism in response to the presence of such an agent, proportionate to it and to the changes caused by it. May not the reaction of the organism to a sensitizing agent be so extreme that, instead of reestablishing an equilibrium after the agent is neutralized, it continues to react with an intensity which leads to exhaustion and perhaps to a breakdown of function?

#### TREATMENT

The local treatment of the cutaneous lesions seems to be of little value as long as the primary foci in the glands are not cured. For this reason some authors have advocated operative drainage of the prostate gland and the seminal vesicles. Taylor<sup>25</sup> reported favorable results with local applications of elastoplast, which he left on for seven to eleven days.

In the general management of the disease the following treatments have been used with some benefit: (1) autogenous vaccines, by Scholtz<sup>29</sup>, (2) sulfonamide compounds, (3) 1 per cent solution of merbromin intravenously, by Willmott<sup>134</sup>, (4) iodine in large doses, by Morita<sup>31</sup>, (5) neoarsphenamine, by Lojander<sup>87</sup>, (6) massive doses of vitamin A, by Combes and Behrman<sup>113</sup> and (7) hyperpyrexia by typhoid vaccine or by hypertherm, by Willmott,<sup>134</sup> Hazel and Snow,<sup>127c</sup> Epstein and Chambers<sup>52</sup> and Combes, Dietrich and Cohen<sup>26</sup>.

As general supportive measures, infusions, high caloric diet, vitamins and insulin have been recommended.

#### REPORT OF A CASE

A 25 year old soldier was admitted to the hospital on Oct 24, 1944 with an acute gonorrheal urethritis. After receiving 100,000 units of penicillin he was discharged to duty, but the urethral discharge recurred after a few days. On November 6 he complained of pain and swelling in the right great toe, and on November 9 an oozing batwing-shaped erythematous lesion developed in the crotch, and he was readmitted to the hospital on November 13.

He had contracted gonorrhea two years previously, otherwise his history was noncontributory. His last sexual contact was allegedly on October 20.

After readmission on November 13 he received 200,000 units of penicillin. He also was given sulfadiazine, 1 Gm every six hours for four days. On November 15 bilateral catarrhal conjunctivitis developed. On November 16 his temperature was 99 F and thereafter followed a swinging course with daily peaks of 100 F, reaching 102 F on December 27 and then slowly abating. It returned to normal on Feb 1, 1945 and remained so thereafter.

<sup>134</sup> Willmott, C B. "Keratodermie Blennorrhagique" (Vidal), *Arch Dermat & Syph* **13** 17 (Jan) 1926.

Penicillin therapy was continued from November 19, with daily doses of 200,000 units, to Dec 12, 1944. The patient received a total of 5,000,000 units without appreciable results, except for the clearing of the urethral discharge on about November 25.

On November 23 the metacarpophalangeal joint of the left fourth finger, the left knee and the left temporomandibular joints became swollen and extremely painful. On November 25 he complained of pain in the right knee joint, several days later swelling of this joint was noticeable.

The dermatitis of the crotch did not improve in spite of the continued application of hot compresses. Suddenly, on November 27, an erythematous and purpuric exanthema developed, on both feet and hands, which rapidly became



Fig 1—Keratosis blennorrhagica on the eighth day of the eruption. Observe the diffuse hyperemia of the right heel and the tendency of the lesions to occur in groups.

pustular and extremely firm to the touch. Two days later papular lesions were discovered on the hard and the soft palate, and spreading of the exanthema, which later showed a strong resemblance to hyperacute monilial dermatophytosis, was noted on both ankles, legs and buttocks and in the genital region. On December 1 lesions were also discovered on the scalp.

*Description of Lesions*—After the initial erythematous purpuric stage, the feet, legs, hands and buttocks showed pinhead-sized to bean-sized discrete vesicles which rapidly became pustules. The pustules broke open, revealing scanty cheesy contents, and they developed grayish keratotic caps with dirty brown crusts. In their further evolution these lesions became confluent sitting on erythematous, dusky red bases involving large areas of the soles, feet and, later, both knees.

and buttocks. These dusky red, slightly moist areas resembled relief maps and in the final stages were covered with adherent, dry, powdery scales and crusts and on their fringes showed torn and loose horny masses.

The genitals were involved in a batwing-shaped, confluent and freely oozing, erythematous rash which later became dry, dusky red and covered with powdery scales. The prepuce could not be retracted owing to balanitis and oozing dermatitis of the outer surface of the prepuce.

The scalp showed a similar picture, especially on the hair line, and also some vesicles and pustules. Later, the lesions of the scalp strongly resembled seborrhea and also psoriasis.



Fig 2—Eruption of keratosis blennorrhagica on the fifteenth day, eczematoid areas on the hands

On the fingers, involving all the last phalanges, moist erythema was noted on which occasional pinhead-sized transparent vesicles were scattered, resembling acrodermatitis continua. These lesions also assumed later the dry, dusky red aspect. The nails of the fingers and toes gradually became opaque and brittle, and they were raised up from the nail beds by heaped-up material under them.

The hard and the soft palate showed discrete, flat papules with keratotic, grayish rings sitting on erythematous bases suggesting an iris design. These later lesions disappeared on December 24, at which time the temporomandibular joint and the right great toe were also healed.

*Laboratory Data*—On the patient's admission to the hospital, the urethral smear was positive for gonococci. The sedimentation rate of the blood by the Wintrobe method was 46 mm per hour. During the patient's stay in the hospital his erythrocytes ranged from 4,200,000 to 5,250,000, his leukocytes, from 10,000 to 13,150, his polymorphonuclears, from 72 to 84 per cent, and his lymphocytes, from 26 to 27 per cent. His hemoglobin remained approximately 80 per cent. The Kahn reaction of the blood was negative. Results of repeated urinalyses



Fig 3—Photomicrograph of biopsy specimen from the dorsal surface of the left foot on the tenth day of the exanthema. Note the enormous acanthosis, the hyperkeratosis and the parakeratosis as well as the papillary and subpapillary infiltration with leukocytes. Hematoxylin and eosin,  $\times 60$ .

were normal. Between November 29 and December 11 repeated urethral smears and cultures of the blood were negative for gonococci. The culture of seropurulent fluid aspirated from the left knee joint on November 29 showed merely occasional staphylococci. Smears and cultures from the cutaneous lesions on the feet disclosed no gonococci but occasional staphylococci. Cultures from the lesions in the mouth were negative for *Corynebacterium diphtheriae*, and smears from the same

lesions revealed no Vincent's organisms. Smears and cultures from the bilateral conjunctival seropurulent exudates were also negative for pathogens. Roentgenograms showed the involved joints to be normal. The spinal fluid gave a negative serologic reaction, a cell count within normal range, a normal protein content and normal colloidal gold curve.

*Biopsy Report*—Biopsy of a specimen from cutaneous lesions of the dorsal surface of the right foot on December 6 and examined by an army general medical laboratory was reported as follows:

"The intraepidermal space, noted grossly, is formed between layers of a parakeratotic and edematous epithelium. The intercellular spaces around the edges of this bleb form irregular crevices which are filled with polymorphonuclear leukocytes. There are moderate acanthosis and hyperplasia of the subjacent rete pegs. The papillae are heavily infiltrated with histiocytes, a smaller number of polymorphonuclear leukocytes and edema. MacCallum-Goodpasture stains for bacteria are negative. The specific nature of the changes is not suggested, except that similar microscopic abscesses within the epidermis are seen in psoriasis."

The knee joints, the puncture of which yielded seropurulent fluid, never showed extreme swelling and redness, and they cleared up by the beginning of January 1945, although the patient complained of occasional aching.

Besides the bilateral seropurulent conjunctivitis, bilateral keratitis also developed on December 9 together with some superficial ulceration on the right cornea. He was treated with local and supportive measures and was given an occasional five day course of sulfadiazine. The latter seemed to have no effect on the disease.

The patient lost about 30 pounds (13.6 Kg.) within two months. The muscles around the knees wasted away severely. His mental condition was extremely poor, bordering on melancholia and lethargy. He was given 10 units of insulin twice daily from Jan. 15, 1945 until the date of his transfer to a general hospital on March 3. He also received four transfusions of 500 cc. of whole blood. From February 1 until March 3 he was given hot Sitz baths daily and two gentle prostatic massages weekly. About the middle of February his general condition improved and the cutaneous lesions also showed a remarkable improvement. At the time of his transfer to a general hospital on March 3, 1945 for further treatment and disposition, his condition was fair. He had gained weight, and the ocular, articular and cutaneous lesions had cleared up, with good motility of the joints and with slightly reddened and freely sweating areas on the hands and feet.

#### COMMENT AND SUMMARY

Keratitis blennorrhagica, often referred to as gonorrheal keratitis, while a rare disease, is perhaps not so rare as previously thought, as evidenced by the fact that we have been able to collect 166 case reports, including our own, in an exhaustive review of the medical literature. This number of cases exceeds by far the number previously reported.

This disease occurs predominantly in men in the fourth decade of life who have had repeated attacks of gonorrheal urethritis. The mortality of keratitis blennorrhagica is approximately 10 per cent.

The usual sequence of events is an initial chronic gonorrheal urethritis with local complications followed by gonorrheal arthritis. Soon

thereafter the characteristic symmetric lesions of the skin occur, showing a predilection for the extremities, the areas around the involved joints and the genital regions. Rarely the scalp and the mucous membranes of the mouth are involved. Bilateral conjunctivitis and other ocular complications occur frequently. A prolonged systemic reaction ensues, often ending in death.

We have analyzed in detail the numerous conflicting opinions concerning the cause of this grave and spectacular disease. The preponderance of evidence points definitely to a gonorrheal origin in the vast majority of cases, although in about a score of cases no evidence of gonorrheal infection whatsoever has been found.

As far as we can determine from a study of the literature, no author has ever estimated the percentage of cases of keratosis blennorrhagica in which gonococci were demonstrated in the cutaneous lesions. The fallacious belief that gonococci are practically never found in the cutaneous lesions may result from the fact that most authors were successful in collecting less than half a dozen case reports in which gonococci were found in the lesions of the skin. In striking contrast to this, we have found 17 reports of gonococci in the cutaneous lesions in 166 cases of keratosis blennorrhagica, an incidence of approximately 10 per cent. If to these figures are added the cases in which gonococci have been found in nonkeratotic gonorrheal lesions of the skin, then gonococci have been demonstrated in 12.2 per cent of the cases of all types of gonorrheal exanthemas. In contrast to this relatively high percentage, the blood on culture, it seems, only rarely yields gonococci. We have collected from the literature 5 reports of cases of typical keratosis in which gonococci were cultured from the blood and 18 reports of cases of nonkeratotic gonorrheal exanthemas in which the blood contained gonococci. Positive cultures from joints and eyes have been reported only occasionally.

Arthropathic psoriasis bears only a superficial resemblance to keratosis blennorrhagica. There are numerous differential diagnostic points.

In several recent reports Reiter's disease has been confused with keratosis blennorrhagica. In our opinion, a critical analysis of many of the cases in the literature reported as Reiter's disease does not exclude the probability of a gonorrheal infection.

We have reviewed at length the complex theories concerning the manner in which gonococci can produce such a violent and often fatal infection as is seen in keratosis blennorrhagica. The most logical explanation appears to be that, while a bacteremia of short duration develops, the protracted and grave picture of the disease is due to an extreme degree of bacterial allergy to the gonococci and their endotoxins.

We report a classic case of keratosis blennorrhagica in a 25 year old soldier in whom there developed, in order of sequence, chronic gonorrheal urethritis, bilateral conjunctivitis, keratitis and corneal ulcers, polyarticular arthritis, keratotic lesions of the skin, of the hard palate and of the soft palate, and balanitis circinata sicca

In this dawn of penicillin therapy it is of great interest to note that the injection of over 5 000,000 Oxford units of penicillin neither prevented the development of the full-grown picture of keratosis blennorrhagica nor appreciably influenced its course

# RECURRENT GENITO-ORAL APHTHOSIS AND UVEITIS WITH HYPOPYON (BEHCET'S SYNDROME)

Report of Two Cases

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**T**HIS is a report on cases of a recently (1937) described clinical entity of recurrent ulcerations of the oral cavity and genitals and of repeated attacks of uveitis which, in later stages, is associated with hypopyon. The disease of the eyes may lead to complete loss of vision.

Cases of this syndrome had already been reported before 1937. Bluthé<sup>1</sup> in 1908, Adamantiades<sup>2</sup> in 1931 and Dascalopoulos<sup>3</sup> in 1932 observed patients with this triad. In 1937, Behcet<sup>4</sup> gave the syndrome the name of triple symptom complex, when he recognized the inter-relationship of various pathologic processes in one patient. More cases of the triple syndrome or of part of it will, in all probability, be found in the literature reported by dermatologists or gynecologists as cases of recurrent *ulcus vulvae acutum* or, erroneously, of chancroids, by internists and dentists as cases of recurrent oral aphthae and by ophthalmologists as cases of recurrent iritis, iridocyclitis or uveitis with hypopyon. Some of the accompanying manifestations may have been overlooked, since each specialist may have limited his field of observation.

From the Department of Dermatology, Columbia University, College of Physicians and Surgeons

1 Bluthé, L. Zur Kenntnis des recidivierenden Hypopyons, Inaug. Dissert., Heidelberg, D. Straus, 1908

2 Adamantiades, B. Sur un cas d'iritis a hypopyon récidivant, *Ann d'ocul* **168** 271-278, 1931

3 Dascalopoulos, N. Sur deux cas d'uveite récidivante, *Ann d'ocul* **169** 387-393, 1932

4 Behcet, H. Ueber rezidivierende, aphthöse, durch ein Virus verursachte Geschwüre im Mund, am Auge und an den Genitalien, *Dermat. Wchnschr.* **105** 1152-1157, 1937, *Considérations sur les lésions aphtheuses de la bouche et des parties génitales, aussi que sur les manifestations oculaires d'origine probablement parasitaire, et observations, concernant leur foyer d'infection*, *Bull. Soc. franç. de dermat. et syph.* **45** 420, 1938, *Kurze Mitteilung über Fokalsepsis mit aphthösen Erscheinungen am Mund, Genitalien und Veränderungen an den Augen als wahrscheinliche Folge einer durch Virus bedingten Allgemeininfektion*, *Dermat. Wchnschr.* **107** 1037-1040, 1938, *Some Observations on the Clinical Picture of the So-Called Triple Symptom Complex*, *Dermatologica* **81** 73-83, 1940



Most of the fully developed cases were observed in Europe (Behcet <sup>4</sup> in Istanbul, Turkey, Jensen <sup>5</sup> in Denmark, Franceschetti and Valerio, <sup>6</sup> Knapp, <sup>7</sup> Schultheiss-Linder <sup>8</sup> and Mach, Babel and Naville <sup>9</sup> in Switzerland, Whitwell <sup>10</sup> in England, Weekers and Reginster <sup>11</sup> in Belgium, Gilbert <sup>12</sup> in Germany, Weve <sup>13</sup> in the Netherlands, and Cavara <sup>14</sup> in Italy) Recently, two reports were published from Palestine, one from Jerusalem by Ephraim <sup>15</sup> whose patient had ocular lesions of a questionable nature (trachoma?) and the other from Tel Aviv by Berlin, <sup>16</sup> whose patient had fatal complications of the central nervous system Additional reports of cases of the complete syndrome have recently become

5 Jensen, T Sur les ulcerations aphtheuses de la muqueuse de la bouche et de la peau genitale combinees avec les symptomes oculaires (-Syndrome Behcet), *Acta dermat-venereol* **22** 64-79, 1941

6 Franceschetti, A, and Valerio, M L'uverte recidivante (ad ipopion) manifestazione parziale di una sindrome muco-cutaneo-oculare, *Rassegna ital d'ottal* **9** 1-40, 1940

7 Knapp P Beitrag zur Symptomatologie und Therapie der rezidivierenden Hypopyonitis und der begleitenden aphthosen Schleimhauterkrankung Schweiz med Wchnschr **71** 1288-1290, 1941, Zur Therapie der rezidivierenden Hypopyonitis und ihrer Begleitkrankheiten, *Ophthalmologica* **103** 11-14, 1942

8 Schultheiss-Linder, H Beitrag zur Symptomatologie und Therapie der die rezidivierende Hypopyonitis begleitenden Genitalulcera und uber die Beziehung derselben zum Ulcus vulvae acutum Lipschutz und zu den Vitaminen des B-Komplexes, Schweiz med Wchnschr **71** 1290-1293, 1941

9 Mach, R S, Babel, J, and Naville, M Syndromes muco-cutanes avec complications oculaires (erytheme polymorphe, iritis recidivante aphteuse), *Helvet med acta* **7** 552-564, 1941

10 Whitwell, G P B Recurrent Buccal and Vulval Ulcers with Associated Embolic Phenomena in the Skin and Eye, *Brit J Dermat* **46** 414-419, 1934

11 Weekers, L, and Reginster, H Contribution a l'etude de l'iritis recidivante a hypopion (uverte allergique recidivante a hypopion), *Bull Soc belge d'opht*, 1938, no 76, pp 31-44, Un nouveau syndrome Iritis, ulceres aigus de la bouche et de la vulve, sa parente avec l'iritis recidivante a hypopion, *Arch d'opht* **2** 697-705, 1938

12 Gilbert, W Zur Frage der Iridocyclitis mit rezidivierendem Hypopyon ("Iritis septica"), *Klin Monatsbl f Augenh* **71** 409-414, 1923

13 Weve, H Ueber rezidivierende, allergische Staphylokokkenuveitis, *Arch f Augenh* **93** 14-39, 1923

14 Cavara, V Ueber ein besonderes Syndrom, gekennzeichnet durch rezidivierende Hypopyonitis verbunden mit Geschwuren des Mundes und der Geschlechtsteile und mit Hautausschlagen, *Klin Monatsbl f Augenh* **104** 629-644, 1940

15 Ephraim, H Triple Symptom Complex of Behcet Report of a Case, *Arch Dermat & Syph* **50** 37-38 (July) 1944

16 Berlin, C Behcet's Syndrome with Involvement of Central Nervous System Report of a Case with Necropsy, of Lesions of the Mouth, Genitalia and Eyes, Review of the Literature, *Arch Dermat & Syph* **49** 227-233 (April) 1944

available Foss <sup>16a</sup> as well as Rygh <sup>16b</sup> described 2 cases in men, Bechgaard <sup>16c</sup> observed a young man who suffered from Behcet's syndrome preceded by ileitis and Jensen <sup>16d</sup> saw a case of Behcet's syndrome associated with ulcerative hemorrhagic colitis

One of my patients exhibited the fully developed triple syndrome, while the other had lesions only in the mouth and on the vulva Since it may take a long time (twenty-one years in Whitwell's <sup>10</sup> case 3) before the associated process becomes manifest and since all three signs will not in every case be present simultaneously in each patient, instances of genital and oral lesions alone are considered in this paper as belonging to this clinical entity Cavara,<sup>14</sup> Franceschetti and Valerio<sup>6</sup> and Berlin<sup>18</sup> also considered cases in which these two signs were shown as being typical cases of the syndrome There are far too many cases on record of simultaneous or successive occurrence of genital and oral aphthae to consider the existence of the two differently located conditions as coincidental In some reports the genital and oral lesions were recurrent (Popoff<sup>17</sup>, Cole and Driver<sup>18</sup>, Whitwell,<sup>10</sup> cases 2 and 3, Walter and Roman<sup>19</sup>, Michaelis<sup>20</sup>, Grutz<sup>21</sup>, O'Leary<sup>22</sup>, Gray<sup>23</sup>, Wien and

16a Foss, B Die doppelseitige rezidivierende Hypopyon-uveitis, Behcet's Syndrome, *Acta ophth* **19** 293-329, pts 3-4, 1941

16b Rygh, H Aftose stomatititter med stesiedt hendlikke paa Behcet syndrom, *Tidsskr f d norsk lægefor*, 1941, no 10, p 453

16c Bechgaard, P Case of Recurrent Aphthous Stomatitis Accompanied by Conjunctivitis and Ulcerations of Genitals and Skin, *Ugesk f læger* **102** 1019-1023 (Oct 3) 1940

16d Jensen, J S Ulcerous Hemorrhagic Colitis Associated with Behcet Syndrome, *Ugesk f læger* **106** 176 (Feb 24) 1944

17 Popoff, L L'ulcere vulvaire aigu de Lipschuetz comme manifestation particuliere de l'érytheme polymorphe et d'érytheme noueuse, *Bull Soc franç de dermat et syph* **45** 1254-1268, 1938

18 Cole, H N, and Driver, J R Ulcus Vulvae Acutum with Oral Lesions (Periadenitis Mucosa Necrotica Recurrens), *Arch Dermat & Syph* **32** 119 (July) 1935

19 Walter, F, and Roman, I Beitrag zur Kenntnis der hamatogenen Hautmetastasen bei Ulcus vulvae acutum, *Dermat Wehnschr* **90** 705-709, 1930

20 Michaelis, O Ulcères et aphtes recidivants de la bouche et de la vulve, *Bruxelles-méd* **17** 336-341, 1937

21 Grutz Stomatitis et vulvitis aphthosa chronica recidivans (blastomycetica?), *Zentralbl f Haut- u Geschlechtskr* **20** 415-416, 1926

22 O'Leary, P, in discussion on Becker, S W Aphthae, Acne Rosacea, Involvement of the Scrotum and Thigh, *Arch Dermat & Syph* **28** 254 (Aug) 1933

23 Gray, A M H Case of Ulcerative Stomatitis? *Nature, Proc Roy Soc Med (Sect Dermat)* **17** 57, 1924

Perlstein<sup>24</sup>, Kumer,<sup>25</sup> case 2, Jaffé<sup>26</sup>, Fordyce<sup>27</sup>, Berlin,<sup>10</sup> case 2, Schugt<sup>28</sup>, Carol and Ruys<sup>29</sup>, Ebert and Wolff<sup>30</sup>, Matras<sup>31</sup> and Gibson<sup>32</sup>), while in others a single instance of coexistence of the two manifestations was reported (Planner and Remenovsky<sup>33</sup>, Pils<sup>34</sup>, Talalov<sup>35</sup>, Carol and Ruys,<sup>29</sup> case 3, Sarazin<sup>36</sup>, Kumer,<sup>25</sup> case 1, and Chauffard, Brodin and Wolf<sup>37</sup>) The prognosis for patients with genital and oral lesions becomes more serious if one considers the possibility of ocular and other complications

The fact that in various instances other combinations of the triad occur e g, ocular and genital (Blobner<sup>38</sup>) or ocular and oral lesions (Franceschetti and Valerio,<sup>6</sup> case 3, and Cavara,<sup>14</sup> case 2, and Dascalopoulos,<sup>3</sup> case 2)—is further proof that these three signs are manifestations of one disease It would be going too far to consider as abortive forms of the syndrome cases with only one recurrent mani-

24 Wien, M S, and Perlstein, M O Ulcus Vulvae Acutum Associated with Lesions of the Mouth, *J A M A* **98** 461-466 (Feb 6) 1932

25 Kumer, L Ueber Haut- und Mundschleimhauterscheinungen beim Ulcus vulvae acutum, *Dermat Ztschr* **57** 401-411, 1930, Zur Frage des Ulcus vulvae acutum, *Zentralbl f Haut- u Geschlechtskr* **31** 417, 1929, *Arch f Dermat u Syph* **160** 97-98, 1930

26 Jaffe, K Ulcus vulvae acutum mit aphthenähnlichem Ulkus an Zunge, *Dermat Wchnschr* **90** 691, 1930

27 Fordyce, J A, in discussion on Fox, H Aphthous Stomatitis of Twenty-Three Years' Duration, *Arch Dermat & Syph* **2** 256-257 (Aug) 1920

28 Schugt, P Ulcus vulvae acutum (Lipschutz) und seine Atiologie, *Ztschr f Gynak* **49** 2180-2185, 1925

29 Carol, W L L, and Ruys, A C On Aphthosis and Ulcus Vulvae Acutum, *Acta dermat-venereol* **9** 123-141, 1928, Over aphthosis en ulcus vulvae acutum, *Nederl tijdschr v geneesk* **1** 396-406, 1928

30 Ebert, M H, and Wolff, M J Vulvitis (Ulcerative) and Stomatitis, *Arch Dermat & Syph* **30** 472-473 (Sept) 1934

31 Matras, A Ueber aphthenartige Mundschleimhautveränderungen beim Ulcus vulvae acutum mit positivem *Bacillus crassus* Befund, *Arch f Dermat u Syph* **166** 491-497, 1932

32 Gibson, Case of Recurrent Buccal and Vulvar Ulcers, *Brit J Dermat* **50** 664-665, 1938

33 Planner, H, and Remenovsky, F Beitrage zur Kenntnis der Ulcerationen am aussern weiblichen Genitale, *Arch f Dermat u Syph* **140** 162-188, 1922

34 Pils, H Ein Beitrag zur Aphthosis, *Arch f Dermat u Syph* **149** 4-8, 1925

35 Talalov, J Z Ulcus Vulvae Acutum Accompanied by Disease of Skin and of Oral Mucosa, *Arch Dermat & Syph* **30** 510-516 (Oct) 1934

36 Sarazin, cited by Brocq, L Traite elementaire de dermatologie pratique, Thesis, Paris, Doin, 1907, vol 1, p 869

37 Chauffard, A, Brodin, P, and Wolf, M Stomatite et vulvite aphtheuses, suivies de troubles dementiels passagers, *Bull et mem Soc med d hop de Paris* **47** 841-844, 1923

38 Blobner, F Zur recidivierenden Hypopyoniritis, *Ztschr f Augenheilk* **91** 129-139, 1937

festation, such as repeated attacks of severe oral aphthae. The ultimate course of the disease in these patients, or more knowledge of the cause of the syndrome, however, may show that their cases also belong to the entity under discussion.

#### REPORT OF CASES

CASE 1—J. T.,<sup>39</sup> a single man of Italian parentage, born in the United States was first seen in the Eye Institute<sup>40</sup> in 1941, at the age of 21. He gave a history of urethral discharge some years previously, with swelling of the testicles. He repeatedly had sores on the genitals and sores of the gums and lips and had "kernels" in both inguinal areas in 1936. He admitted frequent intercourse with prostitutes. In January 1939 the left eye became inflamed, and one week later the right eye also became inflamed. An operation (pansinusectomy) was undertaken, and for a short time improvement of the condition of the eyes was noted. Cultures from the antrum yielded a type XXIX pneumococcus. Attacks of severe pain in both eyes recurred fairly frequently, however, and in 1941 hypopyon of the left eye was observed for the first time. Iridectomy of both eyes in July 1941 and cyclodiathermy of the left eye in September 1941 did not stop the ocular process. A diagnosis of uveitis with hypopyon was made. Cultures of material from the left conjunctiva yielded *Staphylococcus aureus*.

In September 1941, the vitreous of the right eye was cloudy, and there was a large area of choroiditis in the macular area. Down and temporally, there were white bands of proliferation of retinal tissue. The left eye showed dense opacity of the lens. The fundus was not seen, and no reflex was obtained. There were many floaters in the vitreous. Treatment with atropine, sulfadiazine, sulfathiazole and injections of typhoid vaccine may have had some effect on the hypopyon present, but attacks of pain with hypopyon recurred about every three to four weeks. In October 1941, the left eye was enucleated. Attacks of hypopyon of the right eye continued. In March 1942, the vision of the right eye was 15/200.

The main features of the pathologic report were the following. There was striking infiltration of the iris by polymorphonuclear leukocytes. The ciliary body, the lower portion of the choroid, the retina and the optic nerve were infiltrated by lymphocytes. The retina was completely detached, and there was detachment of the choroid and of the posterior portion of the ciliary body. There was an exudate extending from the surface of the ciliary body, below and beyond along the interior surface of the iris and across the interior lens capsule to join a lesser band of exudate from the upper ciliary processes. The choroid above showed only a slight cellular infiltration in its interior portion. The episcleral vessels over the lower portion of the globe were surrounded by inflammatory cells.

While in the Eye Institute, the patient had several attacks of pain in both ankles and shoulders. In September 1941, swelling of the right ankle with some puffiness was noted. A roentgenogram disclosed osteoarthritis of a mild degree. In January 1942, the patient suffered from myositis or fibrositis of the back.

39 This patient was presented twice at the New York Academy of Medicine, Section of Dermatology and Syphilis at the October 1943 meeting, (*Arch Dermat & Syph* 50 137 [Aug] 1944) with the diagnosis of left postoperative anophthalmos, uveitis and choroiditis of the right eye, possibly due to the virus of lymphogranuloma venereum and again at the October 1944 meeting, with the diagnosis of Behcet's triple symptom complex. (*ibid* 53 147 [Feb] 1946)

40 Dr. Maynard Wheeler gave me permission to report this case.

In 1941 multiple abscesses of the axillas developed, in 1942 the patient had a low grade chronic sinusitis and the sinuses were irrigated. In May 1942, superficial small ulcerations of the gums were noted. On Aug 28, 1942, genital ulcerations of three weeks' duration were discovered.

Physical examination disclosed a healthy-looking young man. His temperature was normal. He had a scar on the left side of the lower lip. He suffered from mild acne of the face and back and a pyogenic infection of the right big toe. On each side of the scrotum he had a dime-sized crateriform ulceration (fig 1) with no



Fig 1 (case 1)—Ulceration on left side of scrotum

induration of the periphery and with a dirty, purulent base. The inguinal lymph nodes were not enlarged. Three dark field examinations as well as smears for Ducrey's bacillus (*Bacillus ulceris mollis*) and *Bacillus crassus* were negative. Frei and Ducrey tests repeatedly elicited strongly positive reactions. A control test with isotonic solution of sodium chloride produced mild redness. Reactions to the Wassermann and Kline tests were negative on several occasions. Further physical and roentgenologic examination showed that the lungs were normal. Tests with tuberculin in dilutions of 1:100,000 and 1:10,000 elicited negative reactions, in a dilution of 1:1,000 the reaction was positive. The spleen was palpable. The prostate gland was slightly enlarged. No gonococci were found in the prostatic smear. Dental roentgenograms showed no foci. The urine gave negative reactions for albumin and glucose. The white blood cell count ranged between 10,000 and 16,000. The differential white cell count did not show any abnormalities. The serum proteins were 7.4 Gm (albumin 5.3 Gm and globulin 2.1 Gm) per hundred cubic centimeters. The rectal examination showed

normal conditions. Since at that time it was thought that the ophthalmic process was possibly due to the virus of lymphogranuloma venereum, therapy with Frei antigen intravenously and with sulfathiazole orally was instituted. No chill or fever followed the first injection. The vitreous cleared considerably, and a large choroidal lesion was visible. On October 27, while the patient was still under treatment with sulfathiazole and Frei antigen, hypopyon again developed.

When the patient was seen in August 1944, no more attacks of iritis had occurred but only light perception of the right eye was present. He had suffered from recurrent attacks of small lesions in the mouth and showed several aphthous ulcers of the buccal mucosa. He also had several attacks of large genital sores, and when seen in August and September 1944, he had large dirty-looking ulcerations on the right side of the scrotum without inguinal adenitis. He was admitted to the Eye Institute for a course of injections of penicillin amounting to 2,400,000 units. The genital lesions practically healed within four days, his vision improved slightly. While he was under treatment with penicillin, a large boil developed on his back and there was inflammation at the site of some injections of penicillin on the buttocks. The temperature at that time rose to 101 F. Frei and Ducrey tests were repeated and reactions were again strongly positive. The reaction to a control test with isotonic solution of sodium chloride was negative. When the patient was last seen, on Nov. 7, 1944, no new genital or oral lesions had occurred during the preceding five weeks. The condition of the eye had remained unchanged.

CASE 2—E. O'C.,<sup>41</sup> aged 21, a single woman born in New York city of Irish and French-Canadian parentage, has been under observation since 1942. She is next to the youngest of nine children, three of whom died early in childhood. No other member of the family has a similar disease. She has suffered from recurrent mouth lesions since childhood. Menstruation started when she was 14. At the age of 13, she noticed the first vulvar lesions. They have since recurred often. At the beginning they appeared between the menses, lately they have sometimes coincided with the menses. Some attacks begin with chills. Temperatures around 101 F. may persist for a few days. The ulcerations heal with deep scars, leading to destruction of the vulva. At the beginning of the attack a mucous discharge is discernible. Sometimes the inguinal glands of the side involved are inflamed. In former years, attacks were accompanied by severe pains in the left or the right calf. Lately the attacks of oral ulcerations have been extremely severe and so frequent that the patient has not been free from them at all. The patient says that she has not had sexual relations. She has always been in good general health. She has never been absent from New York city for any length of time.

*Examination*—The physical examination revealed essentially normal conditions. Psychiatric studies ruled out the possibility that the lesions were self-inflicted. A roentgenogram showed that the lungs were normal. There was no enlargement of the lymph nodes. The eyes were normal. The tonsils were small and could hardly be considered foci of infection. Examination of the teeth (November 1944) showed that the upper right central incisor and the lower right cuspid were abscessed. They were removed.

*Mouth*—The inner surfaces of the lips, the tonsils, the tongue, the soft palate and the hard palate (and rarely the buccal mucosa) were the sites of superficial or deep tender ulcerations which were covered with an exudate and surrounded by a red halo (fig. 2). The ulcerations had a deep, dirty base. Scars of healed lesions were seen on the tongue, lower lip and soft palate.

<sup>41</sup> This patient was presented at the New York Academy of Medicine, Section of Dermatology and Syphilis, on March 6, 1945, with a diagnosis of Behcet's syndrome, abortive form (?).

Genitals (fig 3) The vulva was the site of an extensive indurative, atrophic and destructive process Both labia majora were extensively scarred The posterior part of each labium majus was removed by plastic operation (1942), and biopsy studies of the tissue were made Both labia minora were enlarged and showed multiple fenestration When the ulceration began, the central portion was necrotic with a surrounding hemorrhagic border Deep ulcerations often measured 5 cm in diameter The base of such a large ulceration was granulating, and the border was infiltrated

The uterus was slightly retroverted and the small adnexa were not felt On one occasion, the cervix was found to be normal and on another to show an erosion



Fig 2 (case 2)—Confluent aphthous lesions of the soft palate

*Laboratory Examination*—The urine did not contain albumin or glucose Repeated Wassermann and Kline tests elicited negative reactions The number of white cells ranged between 11,850 and 15,900 The blood count showed 92 per cent hemoglobin, 4,850,000 red cells and a differential count of 72 per cent polymorphonuclear leukocytes, 22 per cent small and 5 per cent large lymphocytes and 1 per cent mononuclear leukocytes The sedimentation rate was 35 to 40 mm per hour Cultures of blood (during the patient's stay in the hospital) and of material from the throat and the nose showed no growth Blood agglutination tests with *Bacillus typhosus* O and H and with *B paratyphosus* A, B and C gave negative results Reactions to Frei and Ducrey tests were repeatedly negative Tests with old tuberculin in a dilution of 1:10,000 produced negative reactions

*Bacteriologic Studies* Genital lesions Results of dark field examinations and of examinations of scrapings for Donovan bodies and of smears for chancroid

bacilli and for inclusion bodies were all negative. Slides and cultures failed to demonstrate fungi, and autoinoculation tests gave repeatedly negative results. Smears of material from the cervix and the ulceration were negative for gonococci. *B. crassus* was once seen in great numbers in a smear from the genital lesion, it was not found in the biopsy specimen. In a culture of material from the lesions, *Staph. aureus* and *Staph. albus* but no anaerobes were found.

**Oral lesions.** On smears inclusion bodies and *B. crassus* were not seen. In a culture *Staph. aureus*, *Staph. albus* and streptococci were found.

**Virus Studies**<sup>42</sup> Suspensions in isotonic solution of sodium chloride were made from genital and oral scrapings. The suspensions were inoculated into mice, guinea pigs, cotton rats, embryonated hen's eggs and chick embryo tissue cultures of the L<sub>1</sub>-Rivers type. There was no evidence of the growth of any virus.



Fig 3 (case 2)—Vulva showing ulceration (A) of left labium majus, fenestration (B) of left labium minus, fibrous bands (C) and extensive scarring. The posterior part of each labium majus was removed by plastic operation.

**Biopsy** (labium majus, specimen obtained at plastic operation) The granulation tissue at the base of the ulceration was swollen and edematous (fig 4). Areas below the ulceration were the sites of a chronic inflammatory reaction with aggregation of polymorphonuclear leukocytes, lymphocytes and plasma cells. The infiltration was not found in any significant distribution around the blood vessels, which appeared thickened. Giemsa stains did not reveal the presence of any organisms. The histopathologic diagnosis was genital ulceration of unknown cause.

**Course and Treatment**—In May 1942, a plastic operation of the vulva was performed in the Sloane Hospital for Women. For a while the patient had no recurrence of the genital lesions. About one year later, the ulcers began to recur.

42 The virus studies were made by Miss E. Molloy.



fairly often (every three or four weeks) She was successively treated locally with 3 per cent sulfathiazole ointment, potassium permanganate soaks and estrogen cream (genitals) and with a solution of hydrogen peroxide, throat lozenges containing nupercaine, and estrogen cream (mouth) The patient avoided brushing her teeth for several weeks and eliminated chicken, eggs and oatmeal from her diet

General treatment consisted of injections of liver extract, the ingestion of nicotinic acid (100 mg twice daily) and sulfathiazole (2 grains [0.13 Gm] daily

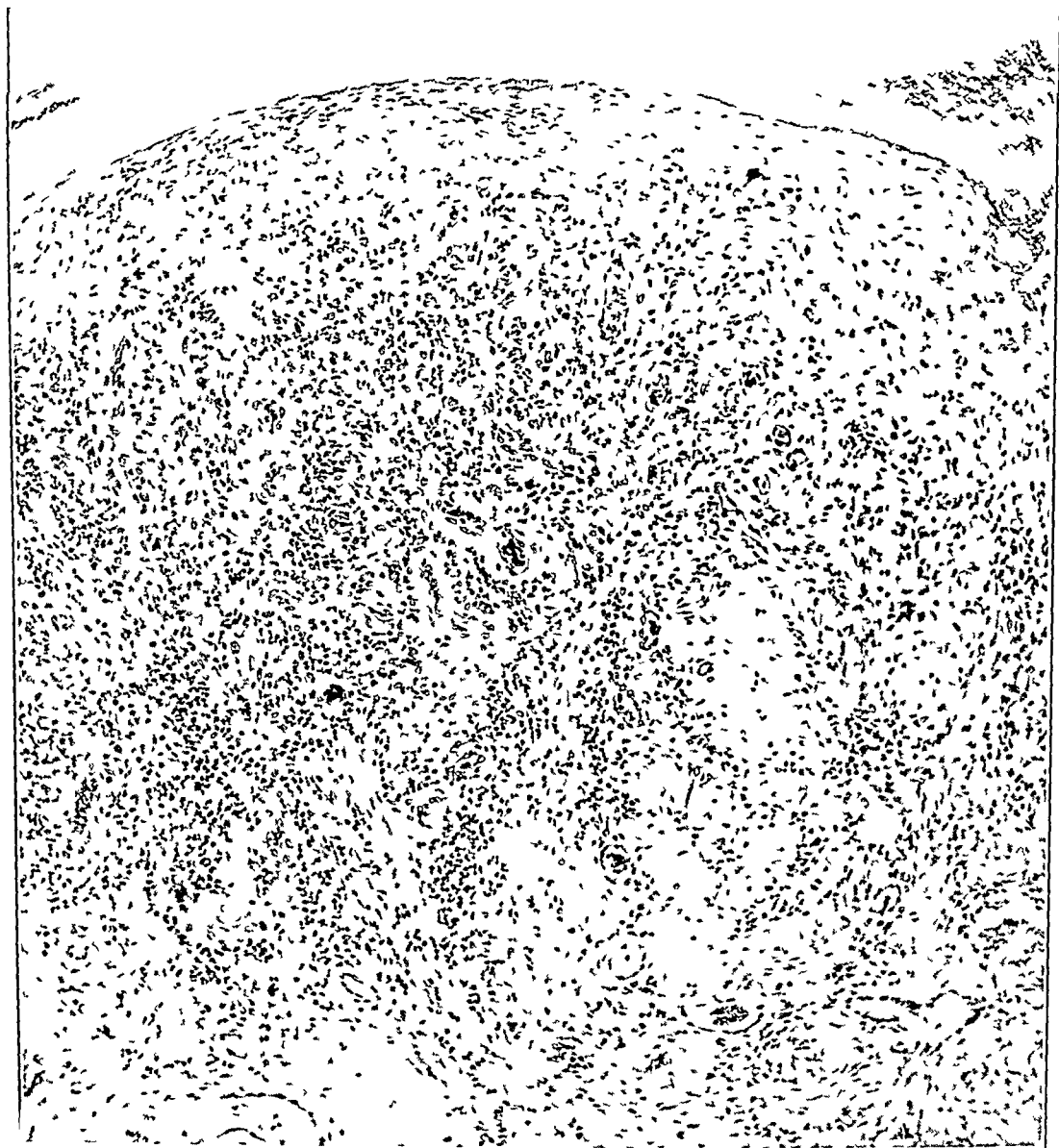


Fig 4 (case 2) —Photomicrograph of ulceration of left labium majus, showing chronic inflammatory reaction below ulceration The specimen was obtained at a plastic operation

for six days), injections of penicillin (1,710,000 units, given at the Presbyterian Hospital), the removal of two abscessed teeth and vaccination for smallpox. Each of these therapeutic attempts was given up when the impression was gained that it made the disease worse rather than better. Under treatment with penicillin especially, the extent of the patient's oral lesions became greater than ever. After the vaccination the patient had no oral lesions for two weeks. There was then a recurrence in the form of deep ulcerations of the uvula and tonsils. The genital lesion which had already been present at the time of the vaccination failed to heal and presented a large 3 by 7 cm deep necrotic ulceration six weeks after the vaccination. With the application of penicillin ointment the lesion slowly became cleaner. Recently, the patient married and became pregnant. She consulted me again in her fourth month of pregnancy. Attacks of oral and genital lesions had become so frequent that several ulcerations in different stages were seen in the oral cavity and on the vulva. Tyrothrycin ointment and others, one of 40 per cent cod liver oil with 1 per cent zinc borosalicylate (Vitaguent) and the second of a bacterial antigen in a base of anhydrous wool fat with zinc oxide, ammonium sulfoichthyolate and sodium borate (Antipeol), were applied locally to the vulval lesions, which subsequently became cleaner. New ulcerations, however, continued to appear. The oral cavity was treated with compound solution of sodium borate. She complained of pain in the lower part of the thighs. Delivery by cesarean section is planned.

#### COMMENT

*Eyes* Involvement of the eye constitutes the gravest manifestation of the triad. It may be the first, second or third and last sign of the disease. The course of the disease of the eyes in the man (case 1) was similar to that observed in other patients. For a while only one eye is involved, later the other eye invariably shows the same changes. In a few instances the disease has started in the two eyes simultaneously. The attacks occur every three to four weeks, or about that frequently. They are characterized by intense periorbital pain and photophobia. The pericorneal reaction is usually mild, there are precipitations in Descemet's membrane. Iritis or iridocyclitis develops later. Either the anterior part of the eye, with or without involvement of the retina and choroid, shows the first pathologic changes, or the posterior parts of the eye manifest retinochoroiditis or periphlebitis (Blobner<sup>38</sup>). In both instances hypopyon is a late symptom. All authors have noted that the hypopyon tends to disappear rapidly (in two to three days), while the vitreous clears slowly and sometimes incompletely. After every attack the vision remaining is definitely diminished. The impairment of the vision progresses to complete blindness in both eyes. Loss of vision is attributed either to posterior synechias with occlusion of the pupil and (secondary) atrophy of the optic nerve (Mach, Babel and Naville,<sup>9</sup> Adamantiades<sup>2</sup>), to secondary glaucoma (Cavara<sup>14</sup>) or to lack of transparency of the vitreous, which cannot recover during the short intervals between the frequent attacks (Franceschetti and Valerio<sup>6</sup>).

Enucleation of one eye, which was undertaken in my patient (case 1) and in patients reported on by Kawabata,<sup>43</sup> Bluthe,<sup>1</sup> Blobner,<sup>38</sup> Weve,<sup>13</sup> Adamantiades<sup>2</sup> and von Hippel,<sup>44</sup> has no influence on the disastrous course of the disease in the other eye

The enucleated bulbus shows infiltration of both the iris and the ciliary body with polymorphonuclear leukocytes and of the choroid with lymphocytes. In most of the bulbi a thick membrane extends through the bulbus, pulling the retina forward (Weve,<sup>13</sup> Blobner<sup>38</sup> and Kawabata<sup>43</sup>). This membrane was missing in von Hippel's,<sup>44</sup> Nakayama's<sup>45</sup> and my patient. The retina is usually found detached, degenerated and infiltrated, and large hemorrhages are seen in front of and behind it. The optic nerve is infiltrated and more or less atrophic. There was no evidence of tuberculosis in any of the histologic specimens, and whatever stains for bacteria were made failed to show organisms (von Hippel<sup>44</sup> and Bluthe<sup>1</sup>). The pathologic observations suggested to von Hippel<sup>44</sup> that the ocular disease was caused by a metastatic pustular process, transmitted through the central vessels of the retina and the long ciliary arteries.

*Erythema Nodosum*—My 2 patients never suffered from erythema nodosum, which occurred in many of the reported cases whether the patients had two or three of the classic symptoms (Jensen<sup>5</sup>, Whitwell,<sup>10</sup> case 2, Weekers and Reginster<sup>11</sup>, Knapp<sup>7</sup>, Koeppe<sup>46</sup>, Sicharulidze<sup>47</sup>, Adamantiades<sup>2</sup>, Blobner<sup>38</sup>, Katznelson<sup>48</sup>, Reis<sup>49</sup>, Pils<sup>34</sup>, Ephraim<sup>15</sup>, Planner and Remenovskiy<sup>33</sup>, Franceschetti and Valerio<sup>6</sup>, Chauffard,

43 Kawabata. Ueber den histologischen Befund einer Iridocyclitis recidivans mit Hypopyon, Chuo-Ganka-Iho **27** 29-32, 1935, abstracted, Zentralbl f d ges Ophth **35** 209, 1936

44 von Hippel, E. Ein Fall von Iridocyclitis mit recidivierendem Hypopyon mit anatomischem Befund, Arch f Ophth **128** 272-279, 1932

45 Nakayama, N. Beitrag zur Kenntnis der pathologischen Anatomie der sogenannten recidivierenden Hypopyonuveitis, Arch f Ophth **116** 249-263, 1925. In his case only one eye was diseased.<sup>1</sup> Oral and genital manifestations were missing.

46 Koeppe, L. Klinische Beobachtungen mit der Nernstspaltlampe und dem Hornhautmikroskop. Ein Fall von doppelseitigem, recidivierenden Hypopyon, kombiniert mit Opticusatrophie, im Bilde der Nernstspaltlampe, Arch f Ophth **94** 267-270, 1917

47 Sicharulidze, I. Zur Frage der recidivierenden Hypopyoniritis im Zusammenhang mit Erythema nodosum, Arkh oftal **8** 658-663, 1932; abstracted, Zentralbl f d ges Ophth **28** 566, 1933

48 Katznelson, A. Recidivierende Hypopyon-iritis und Erythema nodosum, Russk oftal zurn **4** 484, 1925, abstracted, Zentralbl f d ges Ophth **16** 127, 1926

49 Reis, W. Augenerkrankungen und Erythema nodosum, Klin Monatsbl f Augenh **44** 203-224, 1906

Brodin and Wolf<sup>37</sup>, Popoff<sup>17</sup>, Samek and Fischer<sup>50</sup>, Scherber<sup>51</sup>, Mach, Babel and Naville<sup>9</sup>, Dreyer,<sup>52</sup> and Pautrier, Ullmo and Baumeister<sup>53</sup>) Cutaneous eruption was described by Bussalai,<sup>54</sup> Talalov<sup>35</sup> and Michaelis<sup>20</sup> as erythema polymorphe Grutz<sup>21</sup> observed on the extremities doughy infiltrations which discharged a thin, bloody exudate In this case blastomycetes was seen in the tissue

*Rheumatic Pain* Gollwitzer's<sup>55</sup> patient and my female patient complained of drawing pains in the legs whenever a genital sore developed, but there was no redness of the skin Jensen's<sup>5</sup> patient had pains in the forearms My male patient suffered from recurrent attacks of arthritis of the ankles and of fibrositis of the back The patients of Adamantiades,<sup>2</sup> Blobner,<sup>38</sup> Weve,<sup>13</sup> Matras,<sup>31</sup> Popoff<sup>17</sup> (case 1), and Ephraim<sup>15</sup> had more or less severe arthritis, Whitwell's<sup>10</sup> patient (case 1) had acute edema of the leg

*Cutaneous Infections* Various cutaneous infections are described as associated with the syndrome boils (Reis,<sup>49</sup> Gilbert,<sup>12</sup> Cavara<sup>14</sup>), pustules of the forehead (Jensen<sup>5</sup>), pyoderma (Mach, Babel and Naville,<sup>9</sup> Franceschetti and Valerio<sup>6</sup>) and sycotic and seborrheic eczema (Cavara<sup>14</sup>) My male patient had acne of the face, recurrent boils, multiple abscesses of the axilla and at one time some infection of the right big toe The female patient was free of cutaneous infections

*Positive Reactions to Skin Tests* It is interesting to note in connection with these frequent cutaneous infections that some authors find a decided nonspecific hypersensitivity of the skin At least at certain times all intradermal tests may result in a reaction which, in some cases, is indistinguishable from a positive reaction to the test This reactivity was considered to be based on pathergy (Urbach), which does not

50 Samek, J, and Fischer, E Erythema nodosum als bakterielle? Metastase eines Ulcus vulvae acutum, Arch f Dermat u Syph **158** 729-733, 1929

51 Scherber, G Klinik und Bakteriologie der pseudotuberkulösen Geschwüre sive Ulcus vulvae acutum Nachweis der Identität der in den Geschwüren sich findenden Bazillen mit den Scheidenbazillen Doderleins und auf Grund dieser Feststellung Vorschlag, die Geschwürsform Scheidenbazillengeschwüre zu benennen, Arch f Dermat u Syph **127** 359-391, 1919, in discussion on Pautrier, Ullmo and Baumeister<sup>53</sup>

52 Dreyer, in discussion on Pautrier, Ullmo and Baumeister<sup>53</sup>

53 Pautrier, L M, Ullmo, A, and Baumeister, M P Erytheme noueux et ulcere aigu de la vulve de Lipschutz, Bull Soc franç de dermat et syph **45** 1221-1226, 1938, L'erythème noueux aux cours de diverses infections, ibid **45** 1207-1213, 1938

54 Bussalai Ulcus vulvae acutum di Lipschütz, Soc ital di dermat e sif, Boll d sez ital **2** 134, 1934

55 Gollwitzer, M Ueber rezidivierende Hypopyon-Iritis mit Ausgang in doppelseitige Erblindung, Inaug Dissert, Würzburg, Ochsenfurt, Fritz & Rappert, 1938

constitute an antigen-antibody reaction. Even a prick with a sterile needle results in a pustule (Jensen<sup>14</sup>), and on the skin of the genitals the resulting pustule may go on to necrosis. Blobner,<sup>6</sup> Ephraim,<sup>15</sup> Foss<sup>16a</sup> and Jensen<sup>5</sup> elicited reactions to all sorts of intradermal tests and controls with isotonic solutions of sodium chloride. The positive reactions of my male patient to the Frei and Ducrey tests had been considered, on previous occasions when Behcet's syndrome was still unknown to me, as some proof for the diagnosis of chancroid of the genitals and uveitis due to lymphogranuloma venereum. At present, in the light of reports on Behcet's syndrome, this diagnosis seems highly improbable. At no time were chancroid bacilli found in the ulcerations. A picture of recurrent large genital ulcerations which do not possess an undermined border, which as a rule do not cause involvement of the inguinal glands and in which demonstration of the Ducrey bacillus is impossible is not typical of chancroids. If the positive Frei and Ducrey reactions in this case were specific they would refer to some infection with chancroid bacilli and the virus of lymphogranuloma venereum in the past. The patient once had a bubo, and he admitted frequent intercourse with prostitutes. If the positive reactions were nonspecific, it would be hard to explain why results of other tests—for instance, tuberculin in high dilutions and control tests—were negative. (On one occasion an injection of isotonic solution of sodium chloride elicited some redness.) The female patient showed no reactions to repeated tests with Ducrey vaccine and Frei antigen. Apparently, unspecific reactions to various skin tests are not encountered in all cases of the disease. Their occurrence may be seen only in patients with a history of, or in the presence of, spontaneous pustular infections of the skin.

*Genital Ulcerations*—The genital ulcerations were much more destructive in the woman (case 2) than in the man (case 1). They sometimes started with general symptoms (chills and high fever). In the beginning they consisted of large grayish necrotic areas. When the slough disappeared large, well demarcated defects of tissue were visible, which either healed with extensive scarring or, if they occurred on the thin parts of the small labia, with fenestration. For many years the lesions appeared between the menses, later they developed with the menses. Reports in the literature do not permit any conclusions as to the role of menstruation. In the man the occurrence of genital lesions was not accompanied by systemic signs and did not incapacitate the patient. Pain and accompanying symptoms were negligible. The inguinal lymph nodes of the man did not swell, those of the woman did so occasionally.

*Histology*—Histologically, the genital ulceration of the young woman did not show any characteristic changes, owing perhaps to the chronic stage of ulceration in which the biopsy was performed. Popoff<sup>17</sup>

found epithelioid cells with lymphocytes, histiocytes, plasmocytes and mast cells as well as with occasional giant cells. Perivascular round cell infiltration, which Berlin<sup>16</sup> saw in cerebral, ocular and genital lesions of his patient, was not observed in the genital lesion of my female patient. However, infiltration of the episcleral vessels of the man was noted. Kawabata<sup>43</sup> saw perivascularitis of the retina.

*Oral Lesions* The oral lesions were much more fully developed in the female patient. Since childhood she had rarely been free from them. They occurred on the lips, tonsils, tongue, soft and hard palate and only rarely on the buccal mucosa. The base of the ulcers was covered with a grayish exudate, and the margin was usually surrounded by a red halo. They varied from the size of a pinhead to that of a millet seed and were extremely tender. The man only occasionally had tiny white lesions on his gums and his lower lip. Some of the oral lesions left scars. Jensen's<sup>5</sup> patient had twelve oral lesions at one time. While under treatment with penicillin the young woman exhibited confluent large aphthae involving almost the entire soft palate.

*General Condition* Usually the victims of the disease are young people, between 15 and 45 years of age. They appear to be in good health. Sometimes attacks of recurrent ulcerations start with chills and fever (as in the case of the woman when a genital lesion developed and in Gilbert's<sup>12</sup> patient when a hypopyon formed). Carol and Ruys<sup>29</sup> and Michaelis<sup>20</sup> noticed that three days before an attack the patient's liver became hard and enlarged, and they therefore ascribed the disease to some disturbance of the liver. In Knapp's<sup>7</sup> patient multiple sclerosis was also observed. Autopsy of Berlin's<sup>16</sup> patient, who died after a severe cerebral attack, revealed edema of the liver, small multiple foci of inflammation and softening of the brain.

*Bacteriologic Observations* *B. crassus* was found only in the genital lesions of women. The organism could not be recovered from oral lesions of the same woman or, as a rule, from oral and genital lesions in men. These genital ulcerations associated with oral aphthae do not differ from *ulcus vulvae acutum* as it was originally described by Lipschutz<sup>56</sup>. This author had already noted among his patients one in whom oral lesions also were present. His opinion that this occurrence was coincidental was not upheld by other observers, who remarked that a combination of recurrent genital and oral lesions seemed to be the rule. Numerous authors reported that *B. crassus* was found in many of the genital lesions. The bacillus was never, with the exception of Matras'<sup>31</sup> case, found in oral lesions. Matras also saw positive

56 Lipschutz, B. *Ulcus vulvae acutum* (Lipschutz), in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1927, vol. 21, p. 392.

blood cultures and recovered *B. crassus* from cultures of material from the genital lesions. His results were somewhat similar to Samek and Fischer's<sup>50</sup> observation in a case of *ulcus vulvae acutum* without oral lesions, they were able to demonstrate *B. crassus* in the accompanying erythema nodosum (in cultures and histologic slides). These authors also obtained positive cultures of blood. I and all other observers, among them Wien and Perlstein,<sup>24</sup> Walter and Roman,<sup>19</sup> Cole and Driver,<sup>18</sup> Carol and Ruys,<sup>29</sup> Schugt<sup>28</sup> and Jaffe,<sup>26</sup> were able to demonstrate *B. crassus* in the genital lesions but were unable to observe the organisms in the oral lesions. It should be noted that *B. crassus* was also present in the urethral and vaginal secretions of Samek and Fischer's<sup>50</sup> patient, and it can be found in the same location in healthy persons where there is no sign of an ulcer. Positive results were never obtained when human beings were inoculated with cultures of *B. crassus* or with pus from the lesions. It was pointed out by Wien and Perlstein<sup>24</sup> that other factors besides *B. crassus* are apparently necessary for the formation of the ulcer. Either *B. crassus* is only a secondary invader or autoinfection with *B. crassus*, which ordinarily plays the role of a saprophyte, takes place (Lipschutz<sup>56</sup>). In the female patient *B. crassus* was once found abundantly in the genital lesion. In subsequent slides it was not seen, it was not found in the oral lesions or in the blood culture, and it was absent from the biopsy material of the genital ulcer. If, in addition, one considers that similar cases of genital and oral ulcers have been observed in men patients, in whom naturally *B. crassus* is absent, the role of this bacillus as an etiologic factor is of more than doubtful significance.

Behcet<sup>4</sup> found inclusion bodies in smears of material from ulcerations of the skin and the mucous membrane and considered that these observations were proof that he was dealing with a virus disease. Jensen,<sup>5</sup> Franceschetti and Valerio<sup>6</sup> and I could not confirm his results. In one of my patients, virus studies gave negative results. Franceschetti and Valerio<sup>6</sup> expressed a belief that a virus may use the intestinal tract as the portal of entry, since Carrere<sup>57</sup> observed good results from the energetic disinfection of the gastrointestinal tract. Cultures of material from the oral lesions sometimes yield *Corynebacterium pseudodiphtheriticum* (Jensen<sup>5</sup> and my female patient).

*Cultures of Blood*—In some cases positive results from cultures of blood were obtained (Cavara,<sup>14</sup> mildly pathogenic *Staph. albus*, and Adamantiades,<sup>2</sup> *staphylococcus*). Weve<sup>13</sup> referring to the accompanying articular process and erythema nodosum, stated that he considered the disease a manifestation of an allergic state against the *staphylococcus* Foss,<sup>162</sup> who is of the same opinion, regularly saw the onset of the eye

<sup>57</sup> Carrere, L. Iridocyclite purulente recidivante, Bull. et mem. Soc. franç. d'opht. **44** 345-352, 1931.

disease occurring two to three days after injections with staphylococcus toxoid vaccine. Weekers and Reginster<sup>11</sup> were uncertain as to the nature of the agent which causes the allergic reaction. The site of the manifestation develops greater sensitivity with every attack. Gilbert<sup>12</sup> explained the process in the eye as a metastasis and expressed a belief that the patient suffers from some form of sepsis lenta. Cavara<sup>14</sup> stated his opinion that a virus makes the body more susceptible to infections with the staphylococcus.

*Etiology.* Behcet<sup>4</sup> expressed the firm belief that the disease is caused and maintained by a focus of infection. In his patients, treatment of diseased teeth lessened the frequency of attacks. This experience was not shared by many observers who searched for and removed all possible foci. Extraction of diseased teeth did not help in the cases of von Hippel<sup>44</sup> and Michaelis<sup>20</sup> and in the case of my female patient. Pansinusectomy in my male patient in 1937, tonsillotomy and tonsillectomy in Urbanek's<sup>58</sup> case and operation on a maxillary empyema in Weve's<sup>13</sup> patient did not halt the general trend of the disease.

It is only natural that tuberculosis as an etiologic factor in this chronic disease was widely discussed. More or less pronounced signs of tuberculosis were observed in the patients whose cases were reported by Weekers and Reginster<sup>11</sup> (case 1, suspicious apexes), Jensen<sup>5</sup> (hemoptysis), and Dascalopoulos<sup>3</sup> (case 1, hemoptysis, case 2, opacities of the left apex). Some features of Staehli's<sup>59</sup> case of iritis (involvement of one eye only, absence of genital and oral lesions) in a man with generalized tuberculosis make it doubtful that this was a case of Behcet's syndrome. In spite of lack of convincing evidence Gilbert,<sup>12</sup> Kawabata,<sup>43</sup> Ito,<sup>60a</sup> Shigeta<sup>60b</sup> and Nakayama<sup>45</sup> expressed their belief in the tuberculous nature of the disease. Urbanek<sup>58</sup> regarded the manifestations as allergic signs of tuberculosis. Pillat,<sup>61</sup> who observed chronic dysentery in his tuberculous patient, expressed the opinion that a mixed infection with tubercle bacilli and other organisms explains the disease, since formation of hypopyon coincided with attacks of dysentery. Touraine<sup>62</sup> regards Behcet's syndrome as a grave manifestation of "aphthosis." This term covers various diseases with aphthous lesions, which appear in recurrent attacks and are located on the mucous membrane.

58 Urbanek, J. Fall von beiderseitiger recidivierender Hypopyonuveitis, *Ztschr f Augenh* **83** 357-364, 1934.

59 Staehli, J. Zur Frage der endogenen recidivierenden Hypopyon-Iritis, *Klin Monatsbl f Augenh* **34**:721-731, 1922.

60 (a) Ito. *Nippon Gankwa Gakukwai Zasshi* **25** 1082, 1921, cited by Nakayama<sup>45</sup>, (b) Shigeta. *ibid* **28** 516, 1924, cited by Nakayama<sup>45</sup>.

61 Pillat, A., in discussion on Urbanek<sup>58</sup>.

62 Touraine, A. L'aphtose, *Presse med* **46-47** 571-573, 1941.



*Therapy*—Before the era of the sulfonamide drugs and penicillin, general hygienic measures and local treatment of the ocular, genital and oral lesions were tried. The attacks subsided, but the lesions recurred. In the case of the man, the futility of local measures for the eye is clearly demonstrated. Following the suggestion of Knapp<sup>7</sup> and of Weekers and Reginster,<sup>11</sup> sulfathiazole was given to him, with the result that there were no more attacks of hypopyon, but there was continued recurrence of the oral and genital lesions. Sulfanilamide was given orally without effect in Knapp's,<sup>7</sup> and in Franceschetti and Valerio's<sup>6</sup> case. Sulfathiazole did not influence the oral and genital lesions in my case 2. Transfusions, which were of no avail in Cavara's<sup>14</sup> case, proved helpful to Blobner's<sup>38</sup> patient. Following Knapp's<sup>7</sup> suggestion, the woman (case 2) was treated with vitamin B (liver and nicotinic acid), her condition, however, became decidedly worse. While receiving treatment with injections of penicillin she had the severest outbreak of oral lesions ever observed in her. Five weeks after the completion of penicillin treatment the male patient had had no recurrence of oral and genital lesions and the ocular process was quiescent. After the woman was vaccinated with smallpox vaccine she was free from oral lesions for two weeks, but the genital lesions showed at the same time decided exacerbation.

#### SUMMARY

A review of the literature reveals that instances of the fully developed syndrome (recurrent iritis or uveitis with hypopyon and recurrent genital and oral ulcerations) had been observed prior to Behcet's description of the syndrome. The first American case of this disease is described. The patient was a young man with typical lesions of the eye which had led to the enucleation of one eye and to blindness of the other, with recurrent genital ulcerations and with mild recurrent oral aphthae. The case of a young woman with recurrent genital and oral aphthous lesions is also reported. Her case is included in the cases of the syndrome, since the oral and genital manifestations in this case are identical with those seen in cases of Behcet's<sup>4</sup> syndrome. It may take many years before another manifestation of the triad develops. In this case the genital ulceration of the young woman is identical with the lesion described as *ulcus vulvae acutum* by Lipschutz.<sup>56</sup> Bacteriologic studies yielded no clue to the causative factors, and the trial of various therapeutic measures (including the administration of vitamins, the removal of foci, vaccination, the ingestion of sulfonamide compounds and the injection of penicillin) gave no satisfactory results.

35 East Eighty-Fourth Street

## ACUTE LUPUS ERYTHEMATOSUS DISSEMINATUS TREATED WITH PENICILLIN

Report of a Case

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ALTHOUGH the etiologic agent of lupus erythematosus disseminatus is still a matter of controversy, there are some investigators who believe that there is sufficient evidence at the present time to justify the opinion that this disease is caused by streptococci or their products. Streptococci have been isolated from the blood in a number of cases of the disseminated type and O'Leary,<sup>1</sup> among others, is of the opinion that those micro-organisms are of etiologic importance.

If this opinion is correct, it stands to reason that the administration of penicillin should be beneficial to a patient with lupus erythematosus disseminatus. It might be well to recall at this point that similar reasoning was employed when the sulfonamide compounds were first introduced into therapy, and although encouraging results following the oral administration of these compounds have been reported the results in general were disappointing.<sup>2</sup>

Having tried the various known methods of treatment in a case of subacute lupus erythematosus, including the recently advocated internal administration of iodine,<sup>3</sup> and having failed miserably, I decided to give the patient penicillin. The result was so gratifying that the case is here reported.

### REPORT OF CASE

R E D, a 46 year old white man, was referred to me in March 1945 for the treatment of an eruption involving the hands, arms, neck, chest, back and legs, which was of seven months' duration. The patient's past, personal and family histories were irrelevant.

*Present Illness*—In July 1944 the patient had a severe sunburn, following which he noted a slight itching sensation on the chest and arms, but no eruption.

1 O'Leary, P A, in discussion on Belote, G H, and Ratner, H S V. The So-Called Libman-Sacks Syndrome, *Arch Dermat & Syph* **33** 642 (April) 1936.

2 Strakosch, E A, in Spink, W W. Sulfonamides and Related Compounds in General Practice, ed 2, Chicago, The Year Book Publishers, Inc, 1942, chap 12.

3 Cannon, A B. Treatment of Lupus Erythematosus Disseminatus by Internal Administration of Iodine, *Arch Dermat & Syph* **51** 26 (Jan) 1945.

was visible at that time. The first eruption noted by the patient appeared in September, when he observed "red papules" on the hands, arms and neck. His physician then told him that he might have psoriasis, but no treatment was given because the patient had to move to Denver. In February 1945 the eruption started to spread to the chest, back and legs.

*Examination*—Examination showed a well developed and well nourished white man, apparently not seriously ill. The general physical examination (Dr R W Vines) revealed normal conditions, with the exception of a cervical lymphadenopathy. On the dorsa of both hands and on the arms, neck, chest, back and thighs was a maculopapular eruption. The majority of the lesions resembled the iris lesions seen in erythema multiforme. Scaling was seen only in a few lesions.

*Laboratory Data*—Examination of the blood performed on March 30, 1945 showed a hemoglobin content of 90 per cent, 4,680,000 red blood cells and 8,100 white blood cells per cubic millimeter, of which 78 per cent were polymorphonuclear neutrophils and 22 per cent lymphocytes. The sedimentation rate was 27 mm (Westergreen) at the end of the first hour. The Wassermann reaction was negative. The urine and the blood chemistry were normal. A biopsy was performed, and the histologic section revealed edema in the cutis, extravasation of leukocytes and dilatation of the vessels in the papillary bodies.

*Treatment and Further Course*—A tentative diagnosis of erythema multiforme was made, and because the patient complained of pains in the joints he was given sodium salicylate, 3 Gm daily, and a mild antipruritic paste. He was next seen on April 6, at which time the lesions were spreading to the ankles and he complained of general malaise. The lesions were drier, and the scaling was increased, it was at that time that the diagnosis of subacute lupus erythematosus disseminatus was considered. He was then told to live on a high caloric and high vitamin diet and was given 3 Gm of sulfadiazine daily and an iodine-containing ointment. Because the cervical lymph nodes were getting larger, he was referred to an otolaryngologist (Dr G L Pattee) who found that both tonsils were infected and advised tonsillectomy, which was performed on April 9. After the operation the lesions faded considerably, and for the first time no new lesions appeared. Because the patient suffered a severe generalized reaction to the sulfonamide compound, the drug was discontinued and he was given iodine internally as recommended by A B Cannon<sup>3</sup>. After two days of iodine medication a severe itching of the entire skin developed, and the patient started to vomit several times. The iodine was then discontinued, and liver extract was given intramuscularly and vitamin B complex by mouth. By the end of April he had new lesions involving the face (butterfly distribution) and the forehead up to the hair line. He was then caught in a snowstorm and was exposed to the wind and cold for several hours. Subsequently he had chills and a fever, the temperature rising to 104 F, and numerous new erythematous lesions appeared all over the body. The diagnosis of acute lupus erythematosus disseminatus was made, and he was hospitalized for treatment with penicillin. At this time the hemoglobin content was 88 per cent, and he had 5,250 white blood cells per cubic millimeter. He was given 20,000 Oxford units of sodium penicillin intramuscularly every four hours around the clock. After five days of penicillin medication the itching of the skin disappeared, and all the lesions started to undergo involution. A total of 2,000,000 units of penicillin was given over a period of sixteen and a half days. He was then discharged from the hospital, feeling well and with the greater part of the lesions gone, although there was

still slight scaling left on the skin on his hands and neck. He was again seen one month after his discharge from the hospital, at which time the sedimentation rate and the results of all other laboratory studies were normal. At the time of writing his skin shows only depigmentation and hyperpigmentation over most of the parts formerly affected.

COMMENT

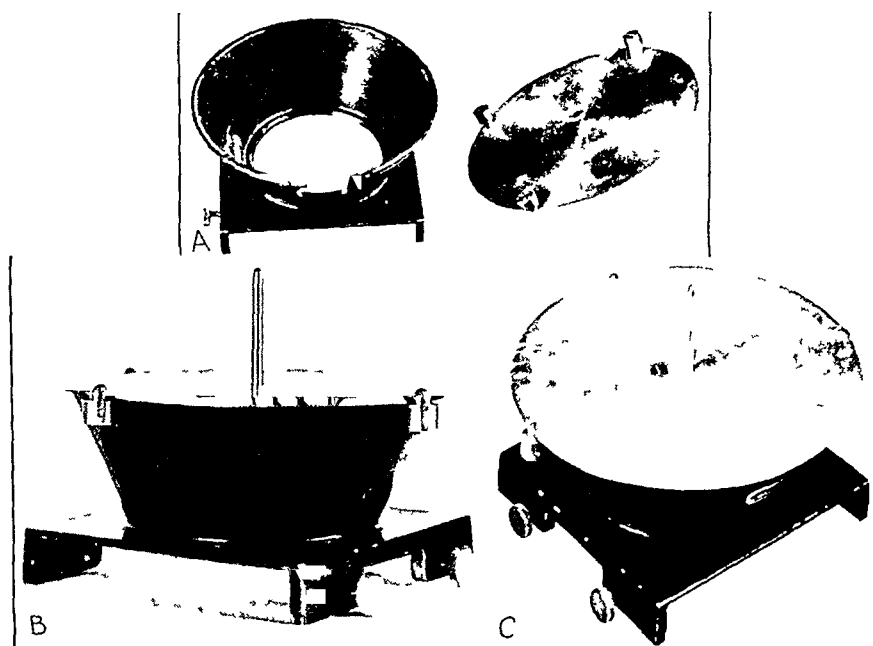
The rapid improvement of the patient suffering from acute lupus erythematosus disseminatus while receiving injections of penicillin may substantiate the theory that this disease is of streptococcic origin. It is realized that the good result obtained in this single case is not conclusive and that further observations with penicillin in the therapy of this disease are necessary before its value can be established.

207 Republic Building

## A DEVICE OF VALUE FOR ROENTGEN RAY EPILATION

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THE PERFORMANCE of roentgen ray epilation for tinea capitis is a technic requiring experience and skill on the part of the dermatologist. Formerly this treatment consumed several hours of time to insure its accurate performance. However, with the addition of various



Device for roentgen ray epilation. *A*, under surface of device and the x-ray cone to which it is attached before the treatment. *B*, side view of attached cone and device. *C*, view from above.

time-saving methods over a period of years, the procedure can now be carried out in less than one hour. Any method which may lessen the technical difficulties or lead to greater accuracy of performance is deemed worthy of report.

For several years, a device has been successfully employed in the dermatologic radiotherapy clinic of Mount Sinai Hospital. It had been

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made in response to a request for some method which would lead to more accurate focusing of the roentgen rays on the five points of the Kienbock-Adamson fields. Prior to this, intersecting silk threads had been placed over the cone in a not particularly satisfactory effort to find the center. With the present method, a wide cone with a focus-skin distance of 15 cm is placed over the portal of an x-ray tube. The device is so constructed as to slide (illustration) over this cone. It consists of a thin circular metal sheet of the same size as the cone. At the edges of this metal sheet are three small metal knobs, which permit the device to slide on and off the cone with ease. In the exact center of this metal sheet is a blunt steel rod which extends downward for an additional 5 cm, thus increasing the focus-skin distance to 20 cm. The roentgen ray technic, accordingly, incorporates a focus-skin distance of 20 cm among its other physical factors.

In the actual performance of the epilation, the child is placed in the proper position and shielded with lead rubber. The device is placed on the cone. The flat surface of the device is then made parallel to the plane of the area of scalp under treatment, with the projecting rod touching the respective Kienbock-Adamson points. The x-ray tube is then locked into position and the device gently removed from the cone. This procedure is repeated for each of the five fields.

Other methods of improved fixation or centering of either the patient or the tube are in use, but this device has proved satisfactory during the performance of hundreds of roentgen ray epilations. For this reason, we are describing its use, with the expectation that other dermatologists may find it of value.

2 East Sixty-Ninth Street

# Clinical Notes

## LYMPHANGIOMA CIRCUMSCRIPTUM

### Successful Results of Treatment with Solid Carbon Dioxide

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BETHESDA, MD

Lymphangioma circumscriptum was first described in 1879 by Tilbury Fox and Colcott Fox, under the title of "Lymphangiectodes,"<sup>1</sup> although Tilbury Fox had given a suggestive description of this disease entity in 1862.<sup>2</sup> The name "lymphangioma circumscriptum" was given to the disease by Morris in 1893,<sup>3</sup> and it seems to be an appropriate one, even though many synonyms appear in the literature. Various forms of therapy have been advocated, varying from roentgen rays to cauterization. Because of the scarring which would result, I decided to use solid carbon dioxide.

#### REPORT OF A CASE

C G, a white woman aged 26, reported that vesicular lesions of the skin developed in the right subscapular area when she was 6 months old. Since that time this area has never been entirely free of the eruption. However, the number of the lesions varied from time to time. Mild trauma resulted first in a clear vesicle which finally became filled with blood. After several days the bloody vesicle fluid was absorbed, and the vesicle again became clear. If a vesicle is ruptured, it continues to ooze for several minutes to half an hour or even longer. The clear vesicular lesions appeared to arise spontaneously, apparently without trauma, on normal skin, they might remain for many weeks, and then they were gradually absorbed. Trauma usually resulted in new vesicle formation.

Routine physical examinations revealed no abnormalities, and results of laboratory tests were within normal limits.

*Dermatologic Examination*—There was a 14 by 20 cm patch of irregularly grouped yellowish and red vesicles and papulovesicles on the right subscapular area. The subcutaneous tissues were unaffected. The vesicles varied from 1 to 8 mm in diameter, some were transparent to yellow, while others were red to purple. Their walls were thickened and were not easily ruptured. When a yellowish vesicle was intentionally ruptured, a clear fluid escaped, this flow

From Dermatoses Section, Industrial Hygiene Division, Bureau of State Services

1 Fox, T, and Fox, T C. On a Case of Lymphangiectodes, *Tr Path Soc London* 30 470, 1879.

2 Pusey, W A. The History of Dermatology, Springfield, Ill, Charles C Thomas, Publisher, 1933, p 126.

3 Morris, M. Lymphangioma Circumscriptum, in Unna, P G, and others. *Internationaler Atlas von seltener Hautkrankheiten*, Leipzig, L. Voss, 1889.

continued for several minutes to half an hour and was in excess to the amount of fluid contained in the vesicle. This fluid was alkaline in reaction to Fisher alkacid tester paper (the test color was yellow-green, indicating a  $p_H$  of 7 to 8). There was some telangiectasia at the base of the clear vesicles (fig 1, *A*).

The skin between the vesicles appeared normal with no scarring at sites of previous lesions.

*Histopathologic Examination*—The area below the epidermis showed large spaces whose walls consisted of a single layer of endothelial cells, apparently lymph spaces. The epidermis immediately above the lymph spaces showed absence

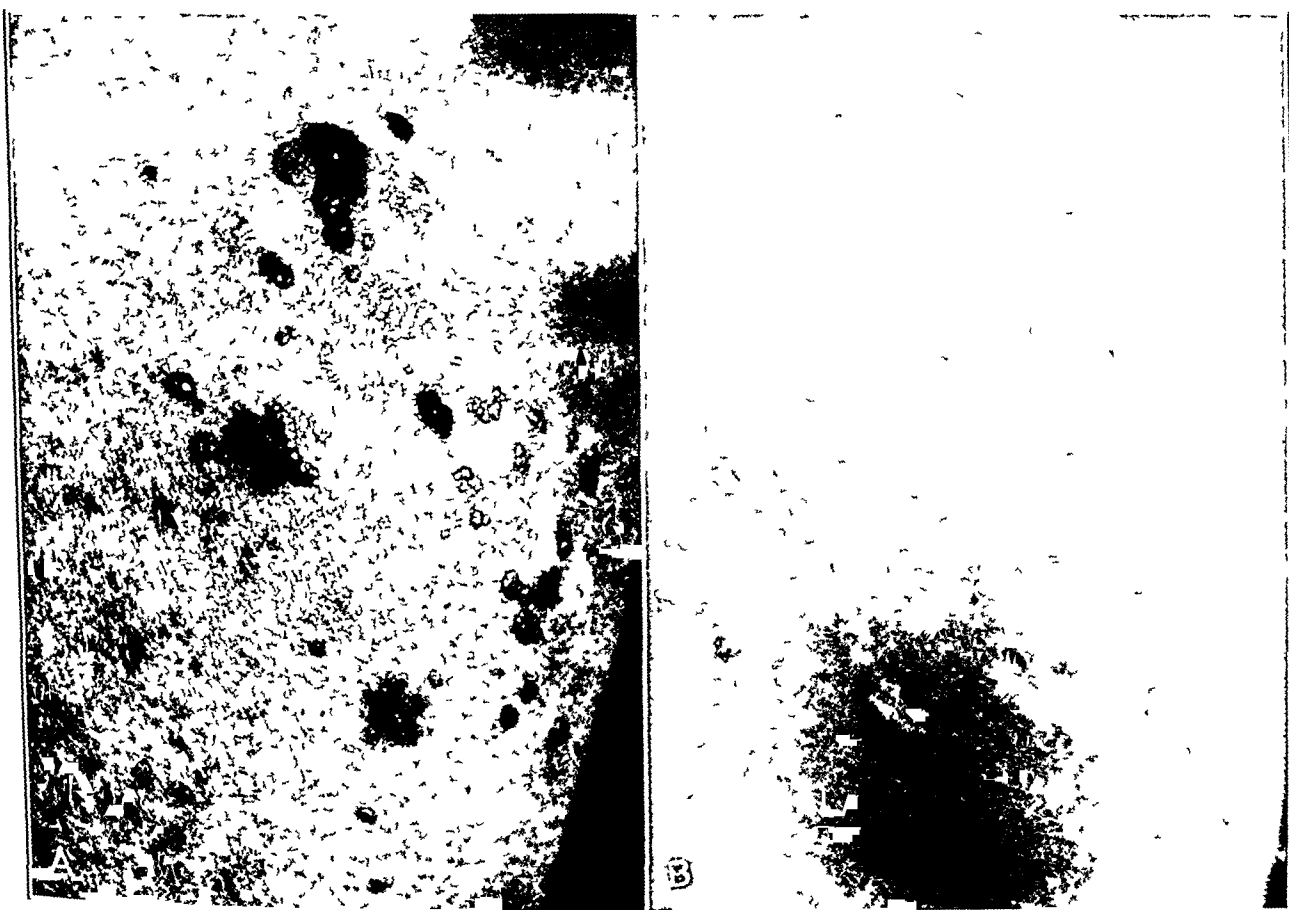


Fig 1—*A*, vesicular, hemorrhagic lesions below right scapular area, *B*, appearance of skin ten months after treatment.

of papillary bodies but otherwise appeared normal. Below the lymph spaces there was a scattered diffuse infiltration with lymphocytes and dilated capillaries. There was also an increase in the fibroblasts and fixed tissue cells (fig 2).

*Clinical Course*—Individual lesions were treated with solid carbon dioxide cut into pencils of irregular shapes. The pencils were so shaped and applied that irregular scarring was produced, thereby the production of a series of regular scars, which would be more noticeable, was avoided. Moderately firm pressure was maintained on individual lesions for forty to sixty seconds.



Treatment was carried out over four months. This was necessary since it was impossible to predict the areas that were pathologic until vesicles developed. Occasionally a lesion had to be treated more than once, but none required more than two treatments.



Fig 2—Photomicrograph showing spaces directly below the epidermis. Hematoxylin and eosin,  $\times 73$ .

Immediately after the freezing, the vesicle became hemorrhagic. This was followed in a few days by crust formation, and in approximately thirty days there remained only a faint white scar (fig 2).

There has been no recurrence of lesions over a period of ten months.

#### SUMMARY

5

The case of a 26 year old woman with lymphangioma *circumscriptum* which had been present since she was 6 months of age is reported. An excellent cosmetic and therapeutic result was obtained with the use of solid carbon dioxide.

1726 M Street, Northwest Washington 6, D C

## A YAWS CLINIC IN NEW GEORGIA

LIEUTENANT COMMANDER LAUREN SOMPAYRAC (MC)

and

LIEUTENANT COMMANDER HARRY SPENCE (MC)

United States Naval Reserve

We were on duty at the United States Naval Hospital at Munda, New Georgia. In the spring and summer of 1944 we noticed symptoms of yaws on the skins of the natives. As we were indebted to these friendly people for the solicitous help they gave our armed forces we felt that we might in some measure repay them by establishing a clinic for the treatment of yaws. The higher echelon permitted us to begin such a clinic at Wana Wana, a native village about an hour and a half by power boat from Munda.

Accordingly, we secured a thatched hut in the sprawling, fly-infested village. Though we were working under primitive conditions, we attempted to work scientifically, yet owing to the exigencies of war our records were lost, only an incomplete graph and some pictures remain. Therefore this can in no sense be considered a scientific paper, rather, it is a setting down of facts remembered because they were so sharply etched in our minds.

Every patient was given a physical examination and a Kahn test. Notes on therapy and progress were taken. We held a total of thirteen weekly clinics, during which we saw more than 300 patients. A reliable laboratory reported that over 95 per cent of these natives had positive serologic reactions. It is interesting that no primary lesions were seen on the genitals. This observation confirmed our belief that yaws is not passed on by sexual intercourse, contrary to a natural suspicion arising from the fact that yaws resembles syphilis. With one exception, a lesion on the buttocks of an infant, all primary lesions were on the faces of children. These primary lesions were fleshy without much induration. Secondary lesions were likewise observed in young people, were maculopustular and were distributed like those of a secondary syphiloderm. We noted that the commonest secondary lesion was observed on the feet of young children, in the form of multiple ulcers. These frequently resulted in a manifestation called "crab yaws," a name originating in the peculiar waddling gait of patients with these painful sores.

We noted bony deformities of the forearm and the condition called "saber shin." Pain in the joints was reported by patients with these symptoms, and it was of interest that in later stages of yaws, especially among the older people, the only symptom of the disease was pain. No changes were observed in the central nervous system or in the heart.

The uncleanness of the natives was a positive factor contributing to the prevalence of the disease, for we found that the clinically well natives were the physically clean natives. The native women, uncomfortably adjusting themselves to European customs, reported to our clinic considerably burdened by dirty layer after dirty layer of pieces of cloth which they had fashioned into a covering supposed to resemble a dress. Visiting them at their homes, we found that they had discarded this covering for the more comfortable gown.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writers and are not to be construed as reflecting the policies of the Navy Department.

wrap-around (*lava-lava*) In spite of the difficult conditions under which we labored, we had many medical volunteers for this clinic Both corpsmen and medical officers were required to wear rubber gloves, although the disease is contagious, fortunately none of the white personnel contracted it

All in all, our results were good We used bismuth preparations and oxophenarsine hydrochloride in dosages recommended by the International Conference on Syphilis All lesions subsided after four injections, with the exception of some ulcers on the ankle which were resistant to the therapy We found that a minimum of eight weekly injections were required for a clinical clearing The serologic reaction was not reversed in a single instance, even after observations based on a total of thirteen weeks of the recommended treatment

No matter how hazardous our mission may have seemed to us at first, we found the natives eager to take our treatment As a matter of fact, our own initial skepticism about their ultimate intentions led us to secure from the British Commissioner both a native Samoan doctor and a guard One might be tempted to say that the natives in some instances were too eager to take what they called the 'needle treatment' On one occasion a young woman was told to bend her arm to hold the alcohol sponge, she returned to her home and came back to us a week later with the arm tightly bound in a sling and with the sponge, now filthy still on the cubital fossa

We held our clinic at Wana Wana from about 9 a m to 3 p m, one day each week Our patients came from the nearby villages on foot and from the adjoining islands in quaintly colorful dugout sailing canoes They cooperated with us in every way possible If our sterilizer was blown out, they would organize a singing group, lustily singing the native version of "Onward Christian Soldiers" After our eighth clinic, the head man of the village had his villagers bring us great quantities of fruit, mats, shells, beads, native fishhooks, walking canes and baskets

That the natives took to us kindly is well illustrated by their daily greeting, "Muna muna Lana," which is their way of saying, 'Good morning!' Some magic, almost mystic, messenger service seemed to apprise the natives of our arrival at the clinic, for after our ride over in the boat loaned to us by the Army for this purpose, we would find the natives lined up, ready for treatment and happily smiling

#### DERMATITIS DUE TO PREPARATION AND ADMINISTRATION OF PENICILLIN SOLUTION

HERMAN GOODMAN, M D, NEW YORK

Reports of dermatitis from penicillin among physicians are unusual Pyle and Rattner gave a short summary of the case of a medical officer<sup>1</sup> One hears of eruptions among workers in factories making and packaging the preparation

##### REPORT OF A CASE

M D, a physician aged 50, a native-born American, had administered penicillin for eighteen months with no damage or irritation On June 15, 1945 he noticed itching, redness, tiny vesicles and oozing in an area  $\frac{1}{4}$  inch (0.6 cm)

<sup>1</sup> Pyle, H D, and Rattner, H Contact Dermatitis from Penicillin, J A M A 125 903 (July 29) 1944

square on the outer side of the middle finger of the right hand. This area corresponded to the site of pressure of the syringe when administering the solution of penicillin. The area involved by the dermatitis increased peripherally until it covered the surface of the outer side of this finger. On June 20 he noticed a similar area on the outer side of the middle finger of the left hand. This corresponded to the site of pressure when the syringe was carried immediately prior to and after administration. Several precautions were taken. The skin was covered with a protective cream and a layer of powder was placed over the cream. Surgical gloves were worn. These gloves were removed in the conventional manner. The wrist of one glove was grasped by the fingers of the other hand, sometimes the left was removed first, and other times the right was removed first. New areas of dermatitis appeared on the inner surfaces of the wrists where contact was made by the fingers of the gloved hands while removing the gloves.

By July 15 these areas were involved: on the right hand, the middle phalanx of the middle finger, the middle joint of the third finger and the inner surface of the wrist, on the left hand, the middle joint of the index finger, the outer surface of the middle finger, the middle phalanx of the third finger and the inner surface of the wrist. Tiny vesicles and itching were noticed at the site of pressure of the bow of the eyeglasses on the left ear. This area corresponded to the section of bow utilized to lift the glasses from the eyes. The left upper lid and the skin of the left infraorbital area became itchy, tiny vesicles appeared, and the skin became darker than normal. Blurring of the sight of the left eye was noticed, and it persisted.

The areas of affected skin were covered with a mixture of bentonite and talc through the vesicular phases. Unfiltered fractional doses of roentgen rays were administered and relieved the itching. All contact with penicillin was stopped. Fresh vesicles ceased to appear, and the oozing stopped. The areas of skin involved in the acute response to the insult with penicillin became denuded and the subkeratin layers scaled. The borders of the lesions on the fingers presented overhanging fringes of keratin. These were cut.

Conventional patch tests with solutions of trademarked sodium penicillin elicited positive reactions. The site of contact was extremely pruritic.

On August 23 the left periorbital area was darker than the right and the sight was slightly blurred. The areas of skin of the fingers were scaly and rough. The wrists showed a slight lichenification with itching, particularly on pressure.

#### COMMENT

The skin of a physician reacted by the appearance of dermatitis venenata after contact with small amounts of solution of conventional penicillin marketed as sodium penicillin. The physician had never previously reacted to any chemical or combination of chemicals. The pH of the solution of commercial penicillin may have been one factor in the production of the dermatitis venenata. The infinitesimal amount of solution of penicillin transferred from the gloved left hand to the skin of the ear caused the appearance of vesicles and intense itching. The solution of sodium penicillin must, then, be a member of the rare group of materials exciting a dermatitis in smallest amount or in lowest concentration in a few persons. Physicians, pharmacists, technicians and others engaged in preparing the contents of vials of sodium penicillin for solution or topical application must consider any irritation of the skin as dermatitis venenata due to penicillin. Precautions should be taken to stop contact on the first appearance of the eruption.

Warning to the patient making topical application of penicillin is also necessary, he should stop the application if the area becomes irritated

NOTE—June 5, 1946 It was learned that the visual fields had been contracted. The physician had become color blind, being unable to distinguish the special color charts in any combination. Despite the avoidance of direct or indirect contact with penicillin, the sites of the original eruptive lesions, middle fingers and third fingers, continue to exhibit dermatitis, itching and slight oozing on exposure to many other things formerly utilized without reaction. On exposure to natural sunlight for half an hour, on May 25, 1946, each of the orbital regions became red, swollen and itchy and continued in diminishing degree until this date. Dark prescription glasses had been worn but afforded no protection.

### SPOROTRICHOSIS

#### Report of a Case of Its Occurrence in California

A. GELBER, M.D., LOS ANGELES

E. H., a white man aged 51, an amateur horticulturist, was first seen on June 2, 1942, when he gave a history of having scratched his left index finger six weeks before while working in his garden. He considered the injury trivial until a hard "pimple" developed at the site of injury and began to ulcerate. Prior to referral he had used topical applications which consisted mainly of compresses of magnesium sulfate and zinc oxide ointment.

Examination revealed a well nourished man whose only abnormality was a bluish red punched-out ulcerated area discharging a serous exudate on the dorsal aspect of his left index finger. There was no ascending lymphangitis on the forearm and no involvement of epitrochlear or axillary nodes. A tentative diagnosis of sporotrichosis was made. Cultures of material taken from the ulcer were made on Sabouraud's medium. Syphilitic gumma was ruled out by failure to observe spirochetes on dark field examination and by negative Wassermann and Kline reactions. Tuberculosis was eliminated by the negative reaction to tuberculin in high dilution and by a roentgen ray examination of the chest and pyoderma by a normal blood sugar level. Coccidioidomycosis was ruled out by direct smears, culture and animal inoculation. Repeated efforts to find the organism on direct smears were unsuccessful. The culture which grew readily at room temperature on Sabouraud's medium yielded *Sporotrichum schenckii* on the seventh day. Microscopically the mycelium appeared as hyaline, fine branching organisms 1 to 2 microns in diameter. The spores were oval to pear shaped and were attached to short lateral branches or longer hyphae, showing rosette configuration. A cutaneous test with sporotrichin antigen 1:10 and a complement fixation test elicited strongly positive reactions. A suspension of the *Sporotrichum* culture was injected intraperitoneally into a male white rat, in which severe orchitis and peritonitis developed. Smears of pus from lesions in testes revealed numerous gram-positive cigar-shaped organisms.

Administration of saturated solution of potassium iodide was instituted within the first few days. A patch test with potassium iodide elicited a negative reaction. The patient had a swelling of the submaxillary node and rhinitis when the 45 mm (28 cc) level was reached. Because of his intolerance to potassium iodide he was given roentgen ray therapy (four unfiltered exposures of 75 r each). On resumption of the saturated solution of potassium iodide a large bleb developed.

medially in the left palm which disappeared when iodides were stopped. Culture of the bleb was negative for *Sporotrichum*, and within a week the swelling subsided and the patient was discharged as cured on Aug 28, 1942.

The patient returned June 9, 1943 with a papillomatous lesion in the medial aspect of the left palm, which had been present for a week. De Beurmann, in one of his cases, noted that "a papillomatous patch of secondary infection developed in the neighborhood of the first lesion." Smears and culture from this area were negative for *Sporotrichum*. The histopathologic observations on biopsy, performed on June 21, 1943, were reported as follows by Dr. Wilbert Sachs:

"At the edge of the section the epidermis is acanthotic, the granular layer is increased, and the horny layer is also increased and densely laminated. At either side of the section the epidermis is missing, and considerable necrosis is present. Throughout the cutis is an intense cellular reaction with numerous small round cells and an occasional plasma cell. No parasites were found."

The patient was discharged on July 13, 1943 and has remained well since then.

#### SUMMARY

A case of solitary lesion of sporotrichosis (sporotrichotic chancre) is reported in which the patient had a nonsporotrichotic papillomatous growth in the palm of the same hand a year later. Although iodide therapy is specific in the treatment of sporotrichosis in cases in which there is an intolerance to iodides, roentgen ray therapy is of value.

Diagnosis of sporotrichosis without cultures is impossible, as the lesion in its various stages may simulate any of the diseases producing granulomatous reactions.

### A FORMULA FOR CRYOTHERAPY FOR ACNE AND POSTACNE SCARRING

ISADORE ZUGERMAN, M.D., PHILADELPHIA

The purpose of this paper is to suggest a modified formula to be used in making carbon dioxide slush for the treatment of acne and postacne scarring.

The benefits, failures, indications, contraindications and methods of use have been discussed in detail by other authors.<sup>1</sup>

My study consisted of the use of slush treatment for acne and postacne scarring on 150 patients, ethyl acetate instead of acetone being used in its formula. The results of treatment were good, definitely paralleling those of Dobes and Keil.<sup>1a</sup>

The substitution of ethyl acetate for acetone was made for the following reasons:

1. A better and longer-lasting slush is obtained, which makes it easier to handle. Ethyl acetate (boiling point, 77° C., specific gravity, 0.900), also a fat solvent, is similar in action to acetone (boiling point, 56.5° C., specific gravity, 0.788) but is less volatile.

From the Dermatologic Service of Dr. A. Strauss, Jewish Hospital, Philadelphia.

1 (a) Dobes, W. L., and Keil, H. Treatment of Acne Vulgaris by Cryotherapy (Slush Method), *Arch. Dermat. & Syph.* 42:547 (Oct.) 1940. (b) Friedlander, H. M. Failure with Cryotherapy in the Treatment of Acne Scars, *ibid.* 46:734 (Nov.) 1942.

2 The odor of ethyl acetate is less objectionable to most patients because of a definite sharp fruity character. It is used commercially in manufacturing fruit essence.

The method of procedure is to grind with a mortar and pestle  $\frac{1}{2}$  pound (227 Gm) of solid carbon dioxide and to add 1 drachm (4 Gm) of precipitated sulfur. This is thoroughly mixed, and then ethyl acetate is slowly added until a semidry slush is formed. The consistency may vary according to individual desires and progress of treatment. It is always advisable to make a thinner mixture early in the treatment because the reaction is not so severe as when thicker mixtures are used. The slush is applied with the pestle, to which several layers of gauze have been attached to the grinding edge by means of an elastic band.

It is recommended that no moisture be allowed to contaminate the ethyl acetate, because it slowly decomposes and acquires an acid reaction. This phenomenon has never been a factor in causing untoward reactions.

There have been no unfavorable reactions directly traceable to the use of ethyl acetate instead of acetone in cryotherapy.

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#### EPILATION BY ELECTRODESICCATION OF HAIRS OF THE SCALP INFECTED BY FUNGI

MAURICE J. COSTELLO, M.D., NEW YORK

Dermatologists have had the experience of finding it difficult to rid the scalp of the few remaining hairs infected by fungi after epilation by roentgen rays. Great difficulty is encountered in removing these infected hairs by manual epilation with tweezers because it is often impossible to grasp the hair which has broken off near or at the surface of the scalp or because it readily breaks under traction when held between the blades of the epilating forceps. Nevertheless, the Department of Health of the City of New York will not permit a child with ringworm of the scalp to return to his classroom if even a single fluorescent infected hair is found in the scalp.

During the past three years, I have overcome the difficulty in epilation by inserting the fine needle of the short wave high frequency current into the hair follicle alongside the infected hair. When the current is turned on, as the needle is withdrawn the infected hair is oftentimes attached to it. This operation should be performed in a dark room with the aid of the Wood fluorescent light. Complete destruction of the hair follicle does not always occur, and a normal healthy hair may later grow from the follicle. Even though as many as a dozen separated hair follicles were destroyed in this manner, the minimum loss of hair would be inconsequential and would not be noticed in the scalp, which is covered by thousands of hairs.

This simple method of destroying infected hairs will permit the return of children to school much earlier than if one had to wait for a similar result by any other method.

140 East Fifty-Fourth Street (22)

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

SULFATHIAZOLE OINTMENT FOR PREVENTION AND TREATMENT OF PYODERMAS OF NEWBORN INFANTS CHARLES A WEYMULLER and ELIZABETH J ITTNER, Am J Dis Child 69 283 (May) 1945

This paper deals with 3,205 newborn infants, each of whom was anointed just after birth with 15 Gm of 5 per cent sulfathiazole in an emulsion ointment base. This preparation was used in an attempt to prevent pustular infections.

Only 4 sporadic cases of pyoderma developed. However, most of these babies were discharged from the hospital seven to ten days after birth. The authors stress that pyoderma in infants is characterized by periods of low incidence. Such facts must be considered in evaluating this prophylactic procedure.

Of the 3,205 infants 49 were readmitted for serious illnesses which required full doses of sulfonamide compounds. In 43 instances the drug employed was sulfathiazole. No instance of sensitization to sulfonamide compounds was encountered. This observation seems to show a low sensitizing power of sulfathiazole in the newborn infant.

NELSON PAUL ANDERSON, Los Angeles

THE TRANSFER OF PENICILLIN INTO THE CEREBROSPINAL FLUID FOLLOWING PARENTERAL ADMINISTRATION WALSH McDERMOTT and R A NELSON, Am J Syph, Gonorr & Ven Dis 29 403 (July) 1945

By dilution techniques of bioassay, no penicillin was demonstrable in the cerebrospinal fluids obtained from 70 patients who had received penicillin in various doses by parenteral routes. The presence of neurosyphilis and, in 1 instance, of tuberculous meningitis did not alter these results.

With the use of an inoculation test for the presence of penicillin approximately 0.02 unit was demonstrable in the cerebrospinal fluid of patients who had received one or two intramuscular injections of 300,000 to 500,000 units of penicillin three to four hours previously.

The failure of the penicillin to appear in the cerebrospinal fluid in appreciable amounts is not due to the fact that it is bound to a high degree to nondiffusible elements in the serum.

The authors suggest that, as the immediate results from intramuscular injection of penicillin for syphilitic meningitis and other forms of neurosyphilis are so promising, it is unnecessary to use the intrathecal route for the treatment of these diseases. On the other hand, in the treatment of purulent meningitis it would seem that on the basis of the available information the administration of penicillin by the intrathecal route cannot be abandoned.

EXPERIMENTAL SYPHILIS IN DIFFERENT SPECIES OF NATIVE AMERICAN MICE UDO J WILE and STURE A M JOHNSON, Am J Syph, Gonorr & Ven Dis 29 416 (July) 1945

All five species of native American mice or their subspecies were found to be capable of harboring syphilitic infections after inoculations with Nichol's strain of *Treponema pallidum* obtained from rabbits. The infection was as readily carried by female as by male mice. On dark field examinations of all material from mice which proved infectious for rabbits no spirochetes were observed. In no instance were any syphilitic changes demonstrable in the inoculated mice.



EXPERIMENTAL SYPHILIS IN THE GOLDEN HAMSTER UDO J WILE and STURE A M JOHNSON, *Am J Syph, Gonorr & Ven Dis* **29** 418 (July) 1945

Pooled emulsions of organs of golden hamsters infected by the intraperitoneal route with *Treponema pallidum* of the Nichol strain obtained from rabbits can be used to produce experimental syphilis in rabbits. Syphilis in hamsters seems to be similar to that which is found in white mice in that the infection remains unapparent. Results of control experiments were negative. The passage of syphilitic infection through the hamster did not increase the virulence of the infection in rabbits, as was noted in mice by the authors.

LATE NEUROSYPHILIS IN NORTH AMERICAN NEGROES AND WHITES WALTER R KIRSCHBAUM, *Am J Syph, Gonorr & Ven Dis* **29** 432 (July) 1945

Clinical and postmortem observations on white and on Negro patients with dementia paralytica are compared. Dementia paralytica occurs, according to the ratio of syphilis, as frequently in the Negro as in the white population in this country. The average age of onset is younger in Negroes, owing to earlier infection. Stationary dementia paralytica in white persons tends to be more chronic and prolonged than in Negroes. More cases of atypical dementia paralytica are observed among Negroes because of concomitant vascular lesions.

In all its varieties, including atrophy of the optic nerve, tabes dorsalis in white patients does not differ from that in Negro psychiatric patients. Only statistics from large city hospitals can settle the question of its frequency among the general Negro population. Organic psychosis due to meningovascular syphilis combined with other disease is more frequently found in Negroes. A high percentage, 44 per cent, of syphilitic aortitis was found in both races. In at least 5 per cent of the cases of dementia paralytica the blood serologic tests elicited negative reactions at the onset, although the tests of the spinal fluid elicited strongly positive reactions at the same time. On the other hand, negative reactions to serologic tests of the spinal fluid together with positive reactions to blood tests have been rarely observed in untreated patients. This paper is concerned only with the Negro population in the United States. The rare incidence of late neurosyphilis among other Negro stocks is acknowledged.

REUTER, Milwaukee

THROMBOCYTOPENIC PURPURA DUE TO MAPHARSEN MARVIN SCHWARTZ and ELMORE C VONDERHEIDE, *J A M A* **128** 657 (June 30) 1945

A case of thrombopenic purpura after thirty injections of oxophenarsine hydrochloride is reported. The platelets in the peripheral blood are probably not destroyed but merely dislocated temporarily into the large capillary beds of the vascular tree, which have been rendered more permeable. No fatalities have been recorded thus far as a result of this complication.

DERMATITIS FROM WEARING APPAREL LOUIS SCHWARTZ and SAMUEL M PECK, *J A M A* **128** 1209 (Aug 28) 1945

Dermatitis has been reported to be caused by fabrics, such as silk, wool and synthetic fibers, by leather, artificial leather, furs, rubber and rubber-containing materials, such as rubber gloves, dress shields, girdles, socks, pajamas and brassieres. Metal and metal alloys, used in jewelry and in eyeglass frames, wrist watches and watch straps, also have caused dermatitis. Plastics, used in spectacle frames, straps for wrist watches, garters and suspenders, have produced dermatitis.

In the majority of the reported cases of dermatitis due to the wearing of fabrics the eruption has been caused by the processed fabrics. Dermatitis among the wearers of fabrics is often caused by the finishes rather than by the dyes. The inner lining of shoes, as well as the backing, contains chemicals which may cause dermatitis. In most cases dermatitis from metallic jewelry has been attributed to nickel. Paraphenylenediamine has been the chief cause of dermatitis from fur.

The eruption begins at the place of contact with the offending material, usually five days or more after the garment has been worn. The patch test is the most practical method for demonstrating the actual cause of a contact dermatitis.

THE TREATMENT OF HERPES ZOSTER BY PARAVERTEBRAL PROCAINE BLOCK THOMAS FINDLEY and REYNOLD PATZER, J A M A **128** 1217 (Aug 25) 1945

Spontaneous and permanent relief from pain was obtained by 4 patients with herpes zoster treated by infiltration of the appropriate sympathetic ganglions with procaine hydrochloride. Block of the regional sympathetic supply relieves herpetic pain by abolishing segmental vasospasm.

BORIC ACID E H WATSON, J A M A **129** 332 (Sept 29) 1945

A boy aged 4½ months, with severe infantile eczema was treated with continuous warm wet dressings of saturated solution of boric acid applied to the entire body. By the second day of this treatment, the skin had improved and boric acid ointment was applied twice daily to all inflamed areas. Three applications were made, a total amount of ointment somewhere between 60 and 100 Gm being used. Sufficient boric acid was absorbed in the twenty-four hour period after the first application to produce convulsions. Blindness and deafness followed. An intense and generalized erythema developed, this was so pronounced that the child was literally the color of a boiled lobster. The patient died three weeks following the onset of the boric acid poisoning. Watson believes that the use of boric acid preparations should be discouraged because of their limited usefulness and the real dangers of their accidental and of their intentional use. Boric acid is a poison.

X-RAY BURNS RESULTING FROM FLUOROSCOPY OF GASTROINTESTINAL TRACT L H GARLAND, J A M A **129** 419 (Oct 6) 1945

During a gastrointestinal fluoroscopic examination by a physician each of 4 patients received serious and temporarily incapacitating burns of the skin over the lumbar area. A small portable x-ray unit was used. X-ray units which are portable and shockproof can be brought much closer to the patient than could the older, heavier, nonshockproof units. A lack of adequate distance between the x-ray tube and the patient's skin is one of the chief sources of danger. If adequate distance, reasonable voltage and low milliamperage, use of a filter, proper speed and dispatch in examination and dark adaptation of the eyes before the commencement of any fluoroscopic work are kept in mind, the average operator is not likely to cause any serious damage.

SKIN DIABETES. HYPERGLYCODERMIA WITHOUT HYPERGLYCEMIA ERICH URBACH, J A M A **129** 438 (Oct 6) 1945

The average sugar level of the human skin is 58 mg per hundred grams. A skin sugar level of more than 68 mg per hundred grams is pathologic. The average ratio between skin sugar and blood sugar is 61 per cent. When the ratio is 70 per cent or more, "independent cutaneous glycolistechia" is present. The term "skin diabetes" is suggested to serve as a designation for the syndrome of a therapy-resistant disease of the skin (furunculosis, abscess of the sweat gland, eczema, pruritus), a high fasting skin sugar level together with a normal blood sugar curve and pronounced improvement of the dermatosis, as well as a fall in the high skin sugar level on a low carbohydrate diet sometimes in combination with insulin.

The high fasting skin sugar levels, the pathologic and characteristically diabetic course of the skin sugar curve following forcing of sugar by mouth and the return to normal of the fasting skin sugar level, as well as of the skin sugar tolerance curve with a low carbohydrate diet notably in connection with insulin, indicate a connection between the clinical syndrome and a disturbance in the carbohydrate metabolism. Not only is sugar in the skin brought there by way of passive diffusion from the blood, but there is also an independent, intermediary carbohydrate

metabolism in the skin "Independent cutaneous glycolistechia" should be regarded as an entity in no way related to the general sugar metabolism of the body and thus unrelated to ordinary diabetes mellitus

**BENZIDINE AS CAUSE OF OCCUPATIONAL DERMATITIS IN A PHYSICIAN** RUDOLPH L BAER, J A M A **129** 442 (Oct 6) 1945

A physician suffered from a severe recurrent eczematous dermatitis on the hands and a milder dermatitis on the face. A test patch with benzidine powder produced a strong eczematous reaction. Each attack of dermatitis had started on a day when the patient had performed a benzidine test for blood in a specimen of stool.

HENSCHEL, Denver

**THE NONANTIGENIC PROPERTY OF BEESWAX** LESLIE N GAY, J Allergy **16** 192 (July) 1945

The author investigated the possible contamination of beeswax by various pollens.

Microscopic examination of crude and filtered "mixed" beeswax revealed no pollens of trees, grasses or ragweed.

Scratch tests with 4 per cent crude and filtered beeswax-arachis (peanut) oil mixtures administered to 12 patients suffering from hay fever or asthma due to one or more varieties of pollens elicited negative reactions. Control tests with similar mixtures to which varying amounts of pollen extracts was added elicited positive reactions. Intracutaneous tests with 4 per cent crude and filtered beeswax-peanut oil mixtures, administered to 31 pollen-sensitive persons, elicited negative reactions.

In the author's opinion beeswax in peanut oil is nonantigenic and is an ideal medium for delaying the absorption of penicillin when administered subcutaneously or intramuscularly. He advises, however, that the beeswax not be kept in solution in a concentration greater than 4 per cent by weight.

MFNDELSON, New York

**SYPHILIS IN INDUCTEES** JACOB ZELLERMAYER, J Ven Dis **26** 194 (Sept) 1945

Among 5,000 men inducted into the armed forces suspected of having syphilis, 570 (11.4 per cent) were proved to be completely free of the disease. Most of these had been suspected of having the disease on the basis of a single blood test, this fact strengthens the concept that a positive serologic reaction alone does not establish the diagnosis of syphilis. Ten and fifty-six hundredths per cent were probably cured of their infection, 1.24 per cent had primary, 0.14 per cent had secondary, 48.84 per cent had early latent and 14.84 per cent had late latent syphilis, 12.98 per cent had complicated syphilis, chiefly cerebrospinal. There was considerable doubt concerning the diagnosis for an additional 6.3 per cent, this shows the need for careful study of the patient before beginning therapy for syphilis.

The group of probably cured patients had received more treatment and more regular treatment than those still having evidences of infection. Nearly 60 per cent of the seropositive patients in the group were found to be previously untreated and to have previously unrecognized infections.

REUTER, Milwaukee

**MYCOTIC INFECTIONS** J G DOWNING and N F CONANT, New England J Med **233** 153 and 181, 1945

Downing and Conant review recent advances in mycotic infections in the light of the changes created by the war in the living habits of large groups of the population. Fungous infections are divided into four major categories: superficial mycoses, dermatomycoses, subcutaneous mycoses and systemic mycoses. In the first category are discussed tinea versicolor, erythrasma, trichomycosis, piedra and otomycosis and in the second category infections due to *Trichophyton*, *Microsporon* and *Epidermophyton*. Unfortunately, recent studies of and suggestions for the

therapy of tinea pedis have not produced as yet a standard method of treatment. Among the subcutaneous mycoses discussed are chromoblastomycosis, maduromycosis and sporotrichosis. Among the systemic are coccidioidomycosis, North American blastomycosis, South American blastomycosis, cryptococcosis, histoplasmosis and actinomycosis.

**PEDICULOSIS CORPORIS AND LEG ULCERS** G. E. MORRIS, New England J. Med. **233** 180, 1945

Morris lists approximately twenty-seven possible diagnoses offered by physicians to explain ulcers of the legs in the middle-aged patient. One, however, is overlooked. Pediculosis corporis is often the underlying cause of multiple ulcers of the legs.

**FALSE-POSITIVE HINTON REACTIONS FOLLOWING CHICKEN POX** L. W. KANE and P. H. HENNEMAN, New England J. Med. **233** 407, 1945

A review of the literature on the subject reveals only 1 questionable report, by Gunn in 1930. Of 22 unselected persons convalescent from chickenpox, 5 had positive Hinton reactions and 1 a positive Kahn reaction. In no case was there a positive Wassermann reaction. These results emphasize the need for a careful evaluation of each case before the patient is subjected to the psychologic trauma of a diagnosis of syphilis and to antisyphilitic treatment.

**PLASTIC SURGERY UPON THE AXILLA IN CERTAIN CASES OF PERSISTENT BROMIDROSIS** K. KAHN, New York State J. Med. **45** 1555, 1945

Kahn reviews the anatomy of the sweat glands and the pathology of bromhidrosis. He has observed a frequency of it as high as 40 per cent in Negro patients and between 6 and 10 per cent in white patients. The offensive axillary odor which persists regardless of hygienic measures is accentuated and becomes decidedly nauseating after intercourse, but only after an orgasm has been completed.

In cases in which the offensive odor failed to respond to soaps, deodorants and antisudorifics, the author has obtained satisfactory results from a blunt dissection and removal of all the gland-bearing subcutaneous tissue in an area previously mapped for the operation according to the number and distribution of the glands. The author's experience has been limited to the use of the sliding graft, which should be the preferred method.

**DERMATOLOGIC ASPECTS OF POLIOMYELITIS** J. G. REYES, New York State J. Med. **45** 1673, 1945

During the recent epidemic of poliomyelitis in New York, Reyes had the opportunity to observe the great frequency of hyperkeratinization in patients suffering from this disease. In 98 per cent of the cases hyperkeratotic lesions were located on both infrapatellar areas, on the anterior and lateral aspects of both ankle joints, on the dorsa of both feet, on both soles and on the malleoli. These lesions, resembling those encountered in cases of vitamin A deficiency, seemed to be proportional in severity to the severity of the poliomyelitis, their prominence disappearing with the abatement of the poliomyelitis. Therefore vitamin A deficiency may be considered as a possible predisposing cause of poliomyelitis. Further investigations are suggested as to the possibility of treating poliomyelitis with vitamin A.

RONCHESE, Providence, R. I.

**RADON OINTMENT TREATMENT OF IRRADIATION ULCERS** ROBERT E. FRICKE and MARVIN M. D. WILLIAMS, Radiology **45**:156 (Aug.) 1945

In 2 cases ulcers due to irradiation, of many years' standing, had undergone malignant change and were treated at Mayo Clinic by the application of petrolatum that contained radon and by highly filtered radium. Since 1930 Uhlmann has advocated the application of radon ointment in the treatment of radiodermatitis.

He has expressed the belief that the mechanism involved is the superficial effect of alpha particles. In the first case reported by Fricke and Williams, evidence of healing had occurred, but further treatment was necessary. In the second case, the ulcer healed completely.

HENSCHER, Denver

UNIVERSAL ALOPECIA B M SCHOLDER and A P MORTON, U S Nav M Bull  
40 348 (Aug) 1945

Scholder and Morton report a case of universal alopecia of eight months' duration in a 19 year old seaman. A neuropsychiatric examination revealed the patient to be suffering from a mild anxiety neurosis, which had been present for two years and had resulted from the shock of identifying the body of his father, who had committed suicide.

Physical, roentgenologic and laboratory examinations revealed normal conditions.

RODIN, South Bend Ind

ERYTHEMA NODOSUM AND OTHER COMPLICATIONS DUE TO INTRACUTANEOUS AND INTRAVENOUS FREI ANTIGEN INJECTIONS C E SONCK, Acta dermat-venereol  
21 473 (May) 1940

The cutaneous manifestation of venereal lymphogranuloma appears usually as an eruption resembling erythema nodosum, occasionally as an eruption resembling erythema multiforme exudativum and rarely as a morbiliform or other type of eruption.

Now that the intracutaneous and intravenous use of Frei antigen in the testing and treatment of venereal lymphogranuloma has become commoner, one can expect to find many more cases of lymphogranulomatous eruptions of the skin. The use of this method of treatment serves to produce the cutaneous manifestations, possibly through an allergic phenomenon.

The author describes 8 cases of erythema-nodosum-like eruption following treatment with Frei antigen and roentgenotherapy. In 4 of his cases there were other factors, such as rheumatic arthritis. In 2 of the cases uncomplicated by any other factors erythema-nodosum-like eruptions followed intracutaneous Frei tests. In 2 other cases the eruptions appeared following intravenously injected Frei antigen and were accompanied with a strong focal reaction in the one and hallucinations in the other. In 1 patient a progressive hyperchromic anemia developed resulting in death following an intravenous injection of Frei antigen. The author believes that in the latter case the therapy was a contributory factor.

PHOTOSENSITIVITY IN LYMPHOGRANULOMA INGUINALE CLINICAL STUDY C E SONCK, Acta dermat-venereol (supp 6) 22 1, 1941

The photosensitivity of 400 patients with venereal lymphogranuloma, evenly divided between males and females, has been investigated. The results have been published in monographic form as an original and primary contribution. At the time of writing, only 1 report of this phenomenon had previously appeared (de la Cuesta), and this report explained the photosensitivity as being due to the antimony used in treatment of the disease.

The manifestations in the cases reported are divided into five stages: (1) subacute inguinal adenitis, (2) chronic inguinal adenitis, (3) chronic ulcer of vulva or penis (fistula of penis), (4) chronic proctitis and (5) genitoanorectal syndrome.

The solar eruptions are produced only by direct sunshine on exposed parts of the body. Attempts to produce the eruption by irradiation with a quartz mercury vapor lamp failed. Women are more susceptible than men. The eruption occurs in 60 per cent of women with chronic and in 30 per cent of women with subacute lymphogranuloma venereum and 12 per cent of men. Not all the exposed parts are equally susceptible. The eruption occurs in the following places, with descending frequency: (1) extensor surfaces of forearms and legs, (2) flexor surfaces of

forearms and legs, (3) extensor surfaces of arms and thighs, (4) flexor surfaces of arms and thighs, (5) neck, nape and sternoclavicular triangle and (6) abdomen, back, hips, face and backs of hands

The eruption varies in appearance from erythematous pinpoint-sized papules to large urticarial wheals, 3 to 7 mm in diameter, and is occasionally accompanied with a diffuse erythema of the affected areas. The eruption is frequently accompanied with moderate or severe pruritus and sometimes with a feeling of discomfort or restlessness. The more sensitive women patients complained of nervousness, nausea and oppression and occasionally of giddiness, headache, chills and numbness of the affected parts.

The photosensitivity appeared five to six weeks after the appearance of the first glandular symptoms and disappeared when the basic disease was cured. In the patients with subacute disease the photosensitivity appeared during a single summer. In the patients with chronic disease the photosensitivity lasted for several years, starting in the spring and disappearing in early autumn, becoming less intense year after year until it finally disappeared. This phenomenon often disappears after a radical operation, such as resection of the rectum. In 6 cases the photosensitivity persisted after all symptoms of the disease had disappeared.

Of the women with chronic lymphogranuloma venereum arthritis appeared in 33 per cent, conjunctivitis in 19 per cent and erythema nodosum in 16 per cent of those who were photosensitive. Of the nonphotosensitive patients arthritis appeared in 19 per cent, conjunctivitis in 7 per cent and erythema nodosum in 4 per cent. Intensely strong Frei reactions occurred in 32 per cent of those with photosensitivity and in 9 per cent of those without this phenomenon.

Investigation into the protein and lipid content of the blood serum, blood counts and urinary porphyrin did not reveal different values for photosensitive patients from those of nonphotosensitive patients.

ROBINSON, Washington, D. C.

ACRODERMATITIS ATROPHICANS OF THE FACE AND THE RIGHT UPPER EXTREMITY  
WITH FORMATION OF NODES. G. MIESCHER, *Dermatologica* 86: 233 (Oct-Nov) 1942.

Four years before seeking treatment a 30 year old man noticed transient bluish red discoloration and edematous swelling below the eyes, of the middle part of the face, of the right elbow and, at a later date, of the right hand and forearm. When seen he complained of rheumatic pain in the right thumb and other joints of the right upper extremity.

The nose, lips and cheeks were decidedly disfigured and of a pale, purplish red hue. The epidermis was thin and somewhat atrophic. The right hand appeared large, and the right thumb was twice the width of the left, the skin showed the same changes as that of the face. A streak of cyanotic discoloration extended from the dorsum of the right hand along the ulnar border to the elbow. Along its course many platelike infiltrations could be felt. The roentgenogram revealed normal bones of the hands and moderate enlargement of the sella turcica. The histologic picture was typical.

The extensive process and the pseudoelephantiasic changes are unusual.

ALOPECIA AREATA MALIGNA TOTALIS. CURE WITH PERANDREN. W. STALDEP, *Dermatologica* 86: 262 (Oct-Nov) 1942.

A 60 year old woman showed in 1940 almost complete loss of hair due to alopecia areata maligna. For a year no growth of new hair was observed in spite of treatment with ultraviolet rays, arsenic, acetylcholine, injections of estrone, and application of ointment and lotions. When twenty injections of 5 mg of testosterone propionate were given in 1941, the hair started to grow in more densely than it had been before the disease.

HELEN O. CURTIS, New York.

# Society Transactions

## LOS ANGELES DERMATOLOGICAL SOCIETY

A Fletcher Hall, M D , *Chairman*

Clement E Counter, M D , *Secretary*

*Jan 9, 1945*

### A Case for Diagnosis (Acanthosis Nigricans?) Presented by DR ANKER K JENSEN

A. S., a white woman aged 67, has hypertensive blood vascular disease with a blood pressure of 188 systolic and 100 diastolic. There is disease of the gallbladder, evidenced by recurrent attacks of pain in the upper part of the abdomen and by roentgenologic examination of a nonemptying gallbladder. About five months ago she noticed a few pigmented areas developing on the sides of her neck. This has gradually spread, until at present both sides and the front of her neck show a mottled pigmentation. Some of the areas are a light brown and others a deeper brown, shading into a dark brown and black. The pigmentation does not extend entirely around the neck in the back. She says that she has not used local applications of cosmetics or other preparations such as ointments or lotions.

#### DISCUSSION

DR KENNETH STOLT I did not arrive at a satisfactory diagnosis. I thought that the eruption might be acanthosis nigricans.

DR HAL E. FREEMAN I believe this is a case of argyrosis. The patient said that she had not used nose drops but that she had used eye drops about the same time the pigmentation developed. She did not know what these eye drops were, but they might have contained silver.

DR SAMUEL AYRES JR I have seen a number of cases of localized argyrosis in the eyes from silver preparations, but I doubt that it is possible to use silver in the eye and get a deposit on the neck and still not show any in the eye. This may be pigmentation from some sort of cosmetic cream. She may have used something with mercury in it, but if that is the explanation for this woman's cutaneous disease why should the pigmentation be limited to the neck and not be present on the face? Also I should like to consider the possibility of a very early acanthosis nigricans. The pigmentation has been present only six months, and it is quite possible that there may be more roughening in the future. There is in this case a definite roughening, not exactly characteristic of acanthosis nigricans or of cutaneous tags, but all around the neck and on the chest are some peculiar little papules, some of which show slight pigmentation. I do not think that one could make a definite diagnosis at present from the clinical picture, but it looks to me more like acanthosis nigricans than anything else I can think of.

DR W. H. GOECKERMAN One cannot entirely exclude pigmentation due to mercury in face cream just because it is around the neck. Several years ago I reported a series of cases of pigmentation due to face cream in which the mercury in the cream was the causative agent. The patients had used it for years. They all had most of the pigmentation around the neck. I think that a biopsy is indicated. If it were found that particles of mercury could be demonstrated in the skin, it would clinch the diagnosis. Further study of the patient's history might help.

DR ANKER K. JENSEN I first thought that the pigmentation was due to the local application of some cosmetic, but there is no history of contact with or of the ingestion of any drug. She refused to allow a biopsy. There is a possibility of early acanthosis nigricans.

**Glomus Tumor** Presented by DR ANKER K JENSEN

F V Γ, a white man aged 58, thirty-one years ago noticed some tenderness on pressure over the right thumb nail. This tenderness has gradually increased in severity. The thumb became so painful in 1927 that it was operated on. No improvement took place after the operation. The right thumb has never been acutely inflamed. Now there is severe acute pain on the lightest touch to the area over the medial side of the base of the right thumb nail. He has developed the habit of carrying the thumb in the palm and protecting it with his fingers. There is a deep red lesion, 3 mm in diameter, at the base of the nail, where the tenderness seems to be the greatest.

## DISCUSSION

DR ROGERS F WAKEFIELD I should like to thank Dr Jensen for presenting this case today, for I have seen this lesion clinically only once before. The history of tenderness and the appearance of the lesion suggest glomus tumor. I agree with that diagnosis.

**Black Hairy Tongue** Presented by DR ANKER K JENSEN

C J D, a white man aged 61, has been having a dry sore throat for the past three months. During that time he has been using different kinds of cough drops and candy type lozenges to relieve coughing. At times he has gone to sleep with such a cough preventive on his tongue. The posterior midportion of the tongue is covered with a dark brown overgrowth of filiform papillae, just anterior to the circumvallate papillae.

No fungous filaments were present in an extemporaneous preparation for direct microscopic examination.

## DISCUSSION

DR M E OBERMAYER The case was a good example of lingua nigra. However, as pseudo black tongue, which is produced by fungi, may have an identical appearance, the possibility of fungi being present should be considered. The relatively short duration of the disease is in favor of the fungus-produced discoloration of the tongue.

DR SAMUEL AYRES JR It is interesting that this man had been holding cough tablets in his mouth for many months because of a chronic sore throat. That is one of the etiologic factors described in connection with black hairy tongue. I do not know what the mechanism is that produces a hairy tongue from the use of cough lozenges. Probably there is some chemical irritation of the papillae. I think that this would be an interesting case to report on later, after cessation of the use of cough drops with no other treatment.

DR NELSON PAUL ANDERSON If black hairy tongue were due to cough drops, one should see many more cases. This statement is not meant to deny the chemical origin of such a disease.

DR M E OBERMAYER Pseudo black tongue is sometimes caused by a streptothrix and at other times by *Microsporon minutissimum*. Dr Weidman was able to produce the disease in a monkey.

DR ANKER K JENSEN I believe that in this case one has an illustration of black hairy tongue due to the chemical irritation of the cough drops that have been used. No fungous filaments were present in the specimens examined.

**Squamous Cell Epithelioma of the Lower Lip** Presented by DR HAL E FREELMAN

Γ R, a man aged 38, a pipe welder smokes cigarets and drinks liquor moderately.

A 'callus' began on the middle portion of the lower lip, two years ago. One year ago while welding he was burned by hot slag on the middle portion of the lower lip. The present tumor has gradually developed to its present size in the past year.



The lower lip is thickened. There is an ulcer in the middle of the lower lip, on the mucous membrane, approximately 13 mm in diameter, and this overlies a firmly and deeply infiltrated area 25 by 13 mm.

The Kolmer and Kline reactions of the blood were negative.

#### DISCUSSION

DR IRVING BANCROFT. I do not see why this tumor could not be removed with a cautery.

DR HAL E. FREFMAN. Slag is a chip of hot metal or rust which flies from the metal as it is burned by the welder's torch.

DR IRVING BANCROFT. I think that this is indirectly an industrial case. It is similar to some of those cases of cancer among primitive races caused by the carrying of hot utensils on the abdomen.

DR CLEMENT COUNTER. I think that this tumor can be removed, and my opinion is that it should have been removed some time ago. I am not at all clear about its connection with compensation. This type of case seems to me much like one of the knotty problems of compensation work. The patient and the insurance company want an opinion. How does one know that there was not a cancer there before the slag hit his lip? That point has to be established.

DR A. FLETCHER HALL. He admits that a callus was there before he was hit by the slag.

DR SAMUEL AYRES JR. I agree with Dr. Counter. Here is a person with a sensitive lower lip. It crusts and peels with sunburn. That is the kind of lip on which cancer will develop. The patient admits that he had a "callus," which evidently antedated the slag burn. I do not think that this case involves a problem of compensation. I saw a man some time ago with an ulcer on his lip, which he said was due to a slag burn. A dark field examination revealed spirochetes, and the lesion was a typical chancre. I certainly believe in giving the man the benefit of the doubt, if there is one, but I do not see how there can be one when he admits having a "callus" before the alleged trauma. I think that it is a prickle cell epithelioma. I would use the high frequency cutting current widely and deeply.

DR J. WALTER WILSON. The best cosmetic result can be got by incision with a cold knife rather than by red hot cautery.

DR FRANKLIN BALL. One must consider what treatment will be necessary after the lesion on the lip is removed and what metastatic lesions may develop. One may grossly understate the necessary treatment when one says simply that this lesion should be removed. A great many considerations are necessary when one outlines the course of treatment in this case. All this has bearing on the industrial responsibility.

DR NELSON PAUL ANDERSON. I do not believe that the industrial aspects of this particular case should be dismissed too readily because of the fact that this man has a thin, sensitive type of skin. In the first place, one does not know that heat has a definite effect, as Dr. Bancroft mentioned. In the second place, when this man goes out in the sun, an actinic cheilitis develops. The conjunctivitis in welders is similar to that produced by the ultraviolet rays from a lamp. Wearing goggles protects his eyes, but his lips are unprotected. The light from the welding arc can definitely aggravate a preexisting lesion.

DR A. FLETCHER HALL. I think that as far as the industrial responsibility is concerned in this case it could be argued all night as to whether or not one burn with slag or from some other source is likely to set up a malignant process on previously conditioned skin. I believe that the Industrial Accident Commission would find this case to be industrial without a doubt, although there is reasonable doubt in my mind. I agree with Dr. Wilson that the best cosmetic result could be expected from excision of a V-shaped wedge and primary suture. I think that radiation would not give as good a result.

DR JOHN D. ROGERS. The history reveals that this man uses cigarettes. The particular type of skin and the history of a little callus present for two years would

make me undecided as to whether or not the slag had anything to do with causing the lesion. I favor the opinion that the type of skin and the use of cigarets are the causative factors.

DR A FLETCHER HALL The history of being "hit by something" is so common in retrospect that it is dangerous to accept that story as bearing on the causation. Last month a man was shown before this society who "thought" that he had been burned on the arm and that a lesion had developed there subsequently. Welders are constantly being struck by burning particles and malignant tumors seldom develop, unless the injury in question was reported by the patient at the time it is difficult to evaluate.

DR ANKER K. JENSEN I think that the lesion should be removed surgically by cautery. I think that any squamous cell epithelioma of the lower lip is best removed surgically and the lip subsequently treated with irradiation.

DR HAL E. FREEMAN In determining the answer to the question of whether or not this is occupational or would be so considered by the Industrial Accident Commission, I was eager to have the opinions of the members. This man did report to the field hospital of his company on Dec. 1, 1943, with a slag burn on this site, and his visit is on record. He himself was fair enough to say that he had had a callus for one and a half years previously, but this was not placed on record at the field hospital. It would not be dishonest to say that this tumor, if not caused by this occupational trauma which is recorded, was possibly aggravated by it. In regard to therapy, if I had what I wanted with which to treat this man, I would consider interstitial radium needles. I have treated cancers of the lip that way with excellent results. I do not agree with the speakers who feel that this tumor should be excised. I think that it will respond well to roentgen rays with proper filtration, and I will show the result of this therapy at a future meeting.

#### A Case for Diagnosis (Atrophic Lichen Planus?) Presented by DR A FLETCHER HALL

E. P., a white woman aged 38, first noticed a group of closely set papules on the ulnar surface of each forearm ten years ago. These patches have remained, and new patches have appeared on the legs and the trunk. They have never itched. New patches of lesions have appeared in the past two years, and these are much more prominent in the past five months. No area once involved has ever cleared.

The ulnar aspect of each forearm, just below the elbow, shows an oval half-dollar-sized group of closely set pinhead-sized papules. Each has light brown pigmentation. The lateral aspect of the left leg has a half-palm-sized, slightly depressed area of light pigmentation and minimal papular elements. The postero-medial aspect of the left thigh and the right side of the chest at the level of the fourth rib show oval palm-sized groups of pinhead-sized pale discrete papules, which are accentuated by stretching the skin. These patches show a tendency to peripheral activity with central clearing. The dorsum of the right hand and wrist show scattered discrete pinhead-sized pale pink papules, each having a depressed glistening center.

The Wassermann reaction of the blood was negative five months ago. The biopsy slide presented with the patient shows only atrophic changes in the epidermis and cornium and is considered not satisfactory because it probably is not a representative specimen.

The patient received six or eight roentgen ray treatments from a dermatologist in Portland, Ore., several years ago. There was improvement but not complete clearing.

#### DISCUSSION

DR CLEMENT COUNTER The diagnosis that suggested itself to me was granuloma annulare with disseminate lesions. Obviously, if that diagnosis were to be proved, it would be necessary that some lesions at least, were slightly raised. In this case all are flat. On the backs of the hands are two or three possibly beginning lesions of that disease, and the patient states that these are the newest lesions.

DR NELSON PAUL ANDERSON I agree with Dr Counter's diagnosis

DR SAMUEL AYERS JR I thought that the disease was a disseminated granuloma annulare. It is rather a different picture from the localized lesions commonly seen on the hands. In this case I think that if one palpated most of the areas one could detect some definite infiltrations.

DR M E OBERMAYER I cannot agree with the suggestion of granuloma annulare. I thought that Dr Hall's diagnosis was clinically well founded, as there was definite atrophy. However, the section showed none of the features of lichen planus. Dr Couperus, with whom I saw the patient, suggested a superficial form of localized scleroderma. After having seen the slide, I am inclined to agree with his suggestion.

DR A FLETCHER HALL Three years ago the patient had five or six roentgen ray treatments by a dermatologist in Portland. This was followed by slight improvement. I feel that the specimen I took for biopsy was not a good one, if I had chosen a different location from which to take the specimen, it might have had more characteristic changes.

#### **A Case for Diagnosis (Lupus Erythematosus?) Presented by DR NELSON PAUL ANDERSON**

According to M J, a white woman aged 50, the present eruption around her eyes started six months ago following a "face peel." She was employed by Douglas Aircraft Company, working under fluorescent lights for fifteen months. During all this time her eyelids were puffy and swollen and the eyeballs were sore and sensitive. Often she applied hot and cold compresses to her eyes for relief. This past summer she took "ultraviolet" treatment and began to get deep circles under her eyes. Following this she had the "face peel."

She has nocturia—micturition two or three times or even every hour—and she has been advised that the walls of her bladder are thickened and enlarged. She had arthritis in her left shoulder and arm while working at Douglas. Late this summer her hands and feet were involved with arthritis. Recently the hips have become involved. She has taken many sun baths.

There is a symmetric purplish, violaceous discoloration of the upper and lower eyelids. There is arthritis in the spine and in the small joints of the fingers, evidenced by enlargements of those joints. There is no evidence of involvement of the muscles in the shoulder girdle.

The hematologic examination showed 16.9 Gm of hemoglobin per hundred cubic centimeters, 5,260,000 erythrocytes and 3,800 leukocytes, with 61 per cent neutrophils, 32 per cent lymphocytes, 5 per cent monocytes and 2 per cent eosinophils. Platelets were normal. Erythrocytes were normal in shape and size.

#### **DISCUSSION**

DR KENNETH STOUT My only suggestion is that some substance used in the "face peel" sensitized the skin around the eyes and that what is seen now may be an actinic effect. I think that it would be a good plan for the patient to wear dark glasses to protect her eyelids.

DR M E OBERMAYER The leukopenia makes me consider the possibility of lupus erythematosus. Such a diagnosis would be in line with Dr Stout's remarks about the precipitating effect of the "face peel."

DR CLEMENT COUNTER In the history of the onset of this "accident" last summer it is stated that the patient had a rather severe erythema for some time, and it is greatly improved over what it was then. This calls to mind a consultation I had a few weeks ago with another woman who had a similar reaction. Accompanying my patient was the woman who did the "peel" procedure. She was emphatic in her statement that this was the first time she had had this type of accident in sixteen years. I am surprised that persons doing such "face peel" procedures do not have more trouble than they do. It seems to me that the

patient I saw could easily have the same appearance as the patient presented here tonight when she gets that far along in the resolution of the reaction to the "face peel"

DR SAMUEL AYRES JR I should not be at all surprised if this discoloration were a form of scar tissue. It has been said that when these chemical "face peels" are used to remove pitted scars there is scar tissue formed which more or less makes the other scars inconspicuous by comparison. I am wondering whether a section might not show changes analogous to a subkeloidal condition which cannot be palpated but which might give rise to this erythema. The margin between the production and the nonproduction of keloids from such chemical "peels" may not be large. Perhaps this discoloration is a subkeloidal scar in which a permanent increase in the small blood vessels or some new formation of fibrous tissue has taken place. The redness may gradually disappear and there may be more scarring. It is too bad that some legal action cannot be taken to prohibit this type of procedure by nonmedical practitioners. There are a number of women doing this sort of work, and they are producing some bad results. They all seem to have the same procedure of applying chemicals and adhesive tape and leaving them on all night. Apparently the Board of Medical Examiners has no control over the situation, but it seems that there should be some way to attack the racket.

DR A FLETCHER HALL I questioned this woman regarding the "peel," and she did not report a violent reaction to it. I could not get the history that there was deep exfoliation. She said that the swelling of the lids had been there for years. She ascribed this to "kidney trouble" which she has had for years. Her complaint seemed to be an indescribable sensation in the affected areas, as though there were "adhesions inside the eyelids." From the appearance of the rest of the skin, it did not look as though much damage had been suffered, and I was doubtful as to whether there was any connection between the "face peel" and her present complaint. In view of the arthritis and the swelling of the eyelids, I could not help thinking of the possibility of trichinosis, and I think that an intradermal test with the trichinella extract should be used.

#### Lymphatic Metastasis of a Cutaneous Epithelioma Presented by DR NELSON PAUL ANDERSON

A B, a white woman aged 62, has had a lesion on the left cheek for about eight years. When she was examined four years ago, she had a small, pea-sized, ulcer on the left cheek about 2 cm from the left ala of the nose. Its base was thickened, but no pearly margin was present. Two years ago she was examined and was said to have a peculiar type of basal cell epithelioma.

Now there is a prominence of the lymphatics in the cheek for about 3 cm around the site of the original indurated pea-sized ulcer. This ulcer is now healed in response to radium treatment. A biopsy specimen shows cancer cells, apparently of the basal cell type but actually somewhat different from the cells usually present in ordinary basal cell epithelioma. There is a lymphatic dissemination of the basal cell type.

#### DISCUSSION

DR M E OBERMAYER The section was interesting because it showed the strands of cancer cells in the lymph spaces.

DR NELSON PAUL ANDERSON The second biopsy specimen which was shown tonight was the one taken from the edge of the lesion in the left malar region.

DR W H GOECKERMAN I wish to ask Dr Anderson whether he believes that this is an unusual type of epithelioma, viewing it now in the light of repeated biopsy examinations. It is an unusual way for a cutaneous cancer to spread.

DR HALE FREEMAN There is already a radiodermatitis present as evidenced by the telangiectasia and atrophy. I believe that this will enter into the consideration of future treatment.

DR NELSON PAUL ANDERSON In retrospect the original lesion was one of those peculiar pearly white button-like epitheliomas one occasionally sees. It is

impossible to state from clinical examination whether such a lesion is a basal cell or a prickle cell epithelioma. Usually radiation therapy is given to see how the lesion responds. Tonight this entire area of pearly white appearance looks as if procaine hydrochloride had just been injected. However, it has slowly and gradually developed over the past year and a half. Definitely this is not a so-called morpheaform epithelioma. It is an example of local lymphatic metastasis of a tumor which histologically resembles a basal cell epithelioma more than any other type of epithelioma. I have never seen this type of local lymphatic metastasis in any basal cell epithelioma. However, this patient has been seen by a physician with considerable experience with cutaneous cancer, who says that he has seen 3 similar instances. Frankly, I feel I am not qualified to make any comments on further treatment. The physician who has seen her in consultation feels that she should have radium needle implants.

### CHICAGO DERMATOLOGICAL SOCIETY

Lester M. Wieder, M.D., *President*

Marcus R. Caro, M.D., *Secretary*

*Jan 17, 1945*

#### A Case for Diagnosis (Vincent's Infection?) Presented by EDWARD A. OLIVER

A white woman, aged 42, presents on the buccal mucosa of the lower lip two oval-shaped infiltrated ulcers. She states that about five weeks ago the lesions began on the left side of the lower lip as a "canker" sore. She bit this, and the ulceration began to increase in size and extent. The lip is swollen, painful and tender to the touch. There are no palpable glands in the submaxillary or submental region. The dark field examination did not reveal spirochetes. The Wassermann and Kahn reactions were negative, and a smear was negative for Vincent's organisms.

#### DISCUSSION

DR. H. E. MICHLLSON, Minneapolis: I do not know just how to classify these ulcers. I have seen similar ones, and I have vacillated between Vincent's angina and erythema multiforme. I believe that there is a form of necrotic aphthous ulcer that is rather similar too. I have no suggestions for treatment.

DR. CLINTON W. LANE, St. Louis: The ulcers in the mouth have necrotic dirty bases with surrounding inflammatory zones and appear much like the ulcers produced by Vincent's organisms. The patient has been adequately treated for Vincent's infection, and despite the few fusiform bacilli which are still present the eruption is probably not a spirochetal infection. On being questioned the patient admitted that for the past few months at frequent intervals she has been taking a proprietary drug for the relief of headache. The present ulcers may be the manifestation of a drug eruption.

DR. MAURICE OPPENHEIM (by invitation): I think that the eruption is a primary lesion of pemphigus. Another case presented this afternoon impressed me as being one of an initial lesion of pemphigus vegetans. Such lesions sometimes appear six months to a year in advance of the cutaneous eruption as I stressed several times in the meetings of this society and in some of my publications concerning primary lesions of pemphigus. I used to consider all such lesions as suggestive of pemphigus, particularly if they did not respond to treatment. In erythema multiforme the lesions of the mucous membranes of the mouth have a much more inflammatory character.

DR. STEPHAN EPSTEIN, Marshfield, Wis.: This patient relates that the lesion in the mouth started as a "canker" sore about five weeks ago. She bit it, and then the stomatitis developed. She has had "canker" sores three or four times a year.

This woman reminded me of a patient of mine with a similar picture of ulcerative stomatitis. Last year the attack started after Christmas, and this year, before. She had been eating peanuts. I wonder if in this case one should not be on the lookout for an allergy to nuts or candy which might have brought on the attack around the holidays.

DR MINNIE OBOLER PERLSTEIN. I should like to offer a diagnosis of periaadenitis mucosa necrotica recurrens of Loblowitz and Sutton. Of the last 4 patients I have seen with this disease, 3 improved with heavy vitamin B therapy. Clinically, all presented the symptoms seen in this patient, except that in some instances there were more lesions on the buccal mucous membrane. The syndrome of recurrent painful necrotic aphthous lesions which heal with scarring is characteristic of the disease of Loblowitz and Sutton.

DR S. W. BECKER. I wonder whether there may not be a factitial element in this case. The patient said that she had used silver nitrate for a long time. I wonder how much of this irritation is due to the irritative treatment.

DR EDWARD A. OLIVER. I am not at all convinced that any one has made the correct diagnosis. The only drug that the patient has taken has been one containing acetylsalicylic acid, acetophenetidin and caffeine, which she occasionally takes for headaches. This lip is painful, and I do not believe that there is any factitial element present. In March she was seen by her family physician, who made a dark field examination, had a Wassermann test made and examined the lesions for Vincent's organisms, all with negative results. Since then I have had a Wassermann test, two dark field examinations and two examinations for Vincent's organisms made without finding anything. Another examination, made by Dr. James H. Mitchell, revealed hemolytic streptococci in pure culture. The lip is definitely infiltrated and the linear ulcers are rather deep. This patient is entirely well now after having had four roentgen treatments of 160 r and boric acid compresses.

**Fox-Fordyce Disease** Presented by DR THEODOR CORNBLEET and (by invitation) DR H. C. SCHORR and DR DAVID COHEN.

J. M., a student nurse aged 18, suddenly began to have an eruption twenty days ago. The changes of the skin are in the axillas and on the pubis. The lesions are small follicular nodules. The background of these shows a faint erythema. There is severe itching. The last menses were scanty but at the predicted time. Previously the flow was more profuse. Nothing else of significance was elicited from the past or present history. The patient is presented because of the recent and sudden onset of the eruption and to ask suggestions as to therapy.

#### DISCUSSION

DR FRANCIS W. LYNCH, St. Paul. I have no therapy to suggest. This patient's menses had always been normal until the last two months, since then the flow has been noticeably scant. I do not know the nature of the endocrine relationship, but I think that there is some such association in this disease.

DR MARCUS R. CARO. In addition to the location on the breasts and pubic area she had a patch of the eruption on the neck and beneath the shoulder strap on the left side. The lesions suggested the presence of an underlying seborrheic factor. I suggest the use of a 40 per cent sulfur ointment as a therapeutic test.

DR THEODOR CORNBLEET. I have tried giving various types of endocrine products in the treatment of the Fox-Fordyce disease without achieving any degree of success. Estrogen, if it had any effect intensified the itching. I am convinced that the correct therapy does not lie in the direction of the estrogens. It is possible that the male sex hormones would be more effective. I have tried them in small doses but so far they have been of no avail. I intend to try them in much larger doses to counterbalance the assumed excessive female sex hormones present in this disease. I have encountered this disease more commonly in Negroes than in white patients. It is noteworthy, too, that Negro subjects have more apocrine glands.

than do others. Furthermore, these structures are more numerous in women. It is suggestive, therefore, that the number of apocrine glands naturally occurring in a group of persons determines the incidence of Fox-Fordyce disease in it. My special reason for presenting this patient with an entity that is not rare was the recent onset of the cutaneous changes and the immaturity as yet of the lesions.

### **Melanoma of the Heel** Presented by DR HERBERT RATTNER

The patient, a white woman aged 55, complains of a lesion on the right heel of six years' duration but with a rapid increase in size in the past two months. The lesion consists of a nodular tumor, the size of a silver dollar, involving the right heel. The tumor presents a bluish black pigmentation and ulceration at the periphery. The patient states that a piece of tissue was removed one year ago. The case is presented for therapeutic suggestions.

#### DISCUSSION

DR RUBEN NOMLAND, Iowa City. I have no therapeutic suggestions, but I think that this case is a good illustration of the fact that a considerable number of malignant melanomas arise from acquired pigmented lesions. From reading the textbooks one gets the idea that most melanotic lesions arise from pigmented moles. It is my opinion that an equal number will arise from acquired pigmented lesions. In 17 cases of malignant melanoma which I have studied and in 13 of which the diagnosis was proved by biopsy, about half the neoplasms arose from acquired lesions. In most of them there were pigmented lesions of the senile type on the back or face, but some arose from other lesions. I think a malignant melanoma that arises from a senile lesion is relatively benign, as this one today is. This woman has had it for six years. Acquired pigmented lesions that undergo malignant change in young people are highly malignant. I do not think that amputation now will do any good, but I think that it is the treatment of choice.

DR S W BECKER. I am glad to have Dr Nomland make that statement. I, too, thought that most melanomas that are acquired develop from a lesion called lentigo maligna. One never knows how long the patient has had this type of lesion. I do not believe that amputation is the treatment of choice. There is one type of operation performed on some patients in which the lesion is removed up into the leg and thigh, including as nearly as possible the lymphatic channels that drain this area. The lymph nodes are dissected from both the femoral and the inguinal regions. It seems to me that that operation would give a reasonable chance of removing the entire process, and, also, if she does have a local recurrence the chances are that it would not spread so rapidly if a great deal of lymphatic tissue has been removed.

DR E P LIEBERTHAL. I suggest radium therapy before surgical intervention is attempted to block off the lymph and vascular channels.

### **A Case for Diagnosis (Angioma Serpiginosum?)** Presented by DR HERBERT RATTNER and (by invitation) DR H RODIN and DR M S KAGEN

A 70 year old white man had a compound fracture of the right tibia twenty-three years ago, followed by osteomyelitis in 1934. During the past six months a dermatitis appeared on the right leg, which has large varicosities. Seven weeks ago, bright red papillary lesions having serpiginous borders and central clearing appeared on the buttocks, in the lumbar area and on the lateral aspects of both thighs. The eruption was bilateral and symmetric. During the past three weeks, the redness and papillary lesions have subsided, leaving suggestions of atrophy. The Kahn reaction was negative. The patient believes that he had similar lesions during childhood.

A histologic specimen is presented.

## DISCUSSION

DR PAUL A O'LEARY, Rochester, Minn. I believe that this patient has purpura annularis telangiectodes as described by Majocchi. The patient not only has purpuric lesions but has in addition, annular telangiectatic plaques with atrophic centers. The unusual feature is the presence of the lesions on the lower part of the abdomen.

DR OTTO H FORSTER, Milwaukee. I agree with the diagnosis of purpura annularis telangiectodes or Majocchi's disease, as offered by Dr O'Leary. I do not think that it is angioma serpiginosum because there is too much pigmentation and atrophy, considering the comparatively short duration of the disease, and primary angiomatous lesions are absent.

### Exudative Dermatitis (?) Presented by DR E P LUBERTHAL and DR I M FRISHER

The patient, a white man aged 36, presented himself at Mandel Clinic of Michael Reese Hospital one month ago with the following history. On March 10, 1943, flat pea-sized dark red sharply outlined lesions appeared on the tip and alae of the nose and on the glans penis and surrounding the urethral orifice. In the course of two months pea-sized, dark red sharply outlined papular lesions appeared on the forehead, and dark red scaly, nodular lesions, from the size of a dime to that of a quarter, on the right cheek, the dorsa of the hands, the flexor and dorsolateral surfaces of the forearm and on the entire surface of the glans penis. The lesions on the glans penis, with the exception of the perimeurethral area, have disappeared completely.

The history reveals that the patient resided for one year, 1939, in British Honduras. He admitted sexual intercourse with native women. In 1942 on the basis of one strongly positive Kahn reaction, his family physician treated him for syphilis with twenty-five injections of neoarsphenamine and the same number of injections of a bismuth preparation administered intramuscularly. On completion of this course of treatment he was pronounced cured of syphilis because of repeatedly negative complement fixation and precipitation reactions.

Pea-sized dark red papular lesions are also present on the scalp. The nodular lesions on the right cheek and occasionally on the forehead reveal exudation.

The Wassermann, Kahn and Eagle reactions have been repeatedly negative. The smears of material from the nose and the serum from a punctured nodule failed to reveal the presence of Hansen's bacilli. The smears from the exudative lesions revealed hemolytic *Staphylococcus albus*. The examination of the blood showed erythrocytes, 4,000,000, and leukocytes, 6,800, with a differential distribution of 42 per cent polymorphonuclear neutrophils, 40 per cent lymphocytes, 8 per cent eosinophils, 9 per cent monocytes and 1 per cent basophils. Determination of blood chemistry revealed nonprotein nitrogen 86 mg, uric acid 71 mg, glucose (fasting) 67 mg and total proteins 6.2 Gm per hundred cubic centimeters. The basal metabolic rate one week ago was -17.5 per cent. The patient had malaria in 1939 while in British Honduras and an intestinal infection which was followed by nephritis.

He has had extensive dermatologic therapy in the last three years which failed to make any impression on the lesions. We have been unable to accomplish any measure of success with various forms of therapy and would appreciate therapeutic suggestions.

## DISCUSSION

DR LOUIS H WINER, Minneapolis. On histologic section the connective tissue showed areas in which the cells appeared foamy. I suggest another biopsy, with staining for fat. The disease may be an extracellular cholesterosis.

DR MAURICE OPPENHEIM (by invitation). I observed this patient two years ago with a similar picture. The lesions were on the hands and arms. I made a diagnosis of dermatophytosis, and today I still think that my diagnosis is right.



I believe that the disease is now a disseminated deep type of dermatophytosis. The histologic observations do not speak against that diagnosis. I think that the patient should be treated with injections of trichophytin.

DR S. ROTHMAN: May I ask whether the possibility of a drug eruption has been ruled out with certainty?

DR E. P. LIEBERTHAL: The history reveals no ingestion of drugs. The histologic structure is typical of exudative dermatitis, however, one has to consider the possibility that previous roentgen therapy may have altered the original architecture of the tissue. Perhaps at a later date this might revert to the original structure. No significance can be attached to previous antisyphilitic therapy, because this was given on the basis of one positive Wassermann reaction two years ago. Frequent repetitions of the Wassermann, Kahn and Eagle tests yielded negative reactions. The patient has received dermatologic therapy with no change in the eruption. The stains made for fungi failed to reveal their presence.

**Severe Stomatitis** Presented by DR EDWARD A. OLIVER and (by invitation) DR ARTHUR GREENBERG

The patient, a salesman aged 56, noticed a grayish white patch on the under surface of his lower lip during the latter part of May 1944. About a week later it spread to the lower part of his tongue. He consulted several dentists, without improvement. During the following five months his tongue became swollen and painful, and the lesions began to ulcerate. He received various forms of local therapy, together with arsenicals intravenously and a course of penicillin elsewhere, which have failed to alleviate the disease. Even though Vincent's infection is present, the cause of the basic lesion is unknown.

The examination reveals an ulcerative stomatitis involving the gums, tongue and mucous membranes adjacent to the teeth, especially the lower jaw. The membrane is excoriated, ulcerated, tender and painful and is covered with an easily removable foul exudate. The tongue is swollen and painful on movement.

The patient has had no elevation of temperature. The Wassermann and Kahn reactions were negative. The blood count was normal and no eosinophils were present. The smears showed spirilla, fusiform bacilli and gram-negative bacilli. The cultures yielded anaerobic long-chained streptococci. No fungi were found.

DISCUSSION

DR RUBEN NOMLAND, Iowa City: This eruption is probably early pemphigus—that is, the initial lesion of pemphigus, which is often an oral lesion. I think that it may be a pemphigus localized in the mouth and that it may remain localized for a long time.

DR EDWARD A. OLIVER: We have watched this patient carefully for the past several weeks. The disease began last May. One thing against the diagnosis of pemphigus was the extreme pain he had suffered, it had been a most painful mouth. The only preparation giving any relief was an iodized phenol mouth wash. Gentian violet medicinal had no effect on the lesions. I believe, as Dr. Oppenheim and Dr. Nomland do, that this may turn out to be pemphigus.

DR OTTO H. FOERSTER, Milwaukee: The thorough application of dry arsphenamine in powder form to the gums and tonsillar fossae rapidly heals Vincent's infections of the mouth, and I suggest its use here.

DR E. P. LIEBERTHAL: I remember 2 cases of this type that Dr. Waldron, of Minneapolis, presented in 1920. He used dilute solution of sodium hypochlorite and removed the infected teeth. He made the point that the solution of sodium hypochlorite was superior to anything he had used previously.

**Epithelioma of Finger (from Trauma?)** Presented by DR CLEVELAND WHITE

I. F., a machinist aged 63 presents a growth at the base of the right index finger at the site of an injury due to a hot steel chip incurred two months ago.

According to his history, which has been checked, the injury was treated by his own physician, who noted no growth at the time, and no foreign body was found on roentgenographic examination. The wound healed. He was not seen by his physician for several weeks, but according to the history the growth appeared after the wound had healed.

The examination at the present time reveals a nodule the size of a hazelnut at the site of the original injury. There is a pearly border and a central depression.

On examination the blood and urine were normal. The Wasserman reaction of the blood was negative. A biopsy has not been performed.

#### DISCUSSION

DR JOHN F. MADDEN, St. Paul: I do not think that a diagnosis can be made without a biopsy. Although the lesion looks more like an epithelioma than anything else, it may not be one.

DR HAMILTON MONTGOMERY, Rochester, Minn.: I thought that clinically the lesion was a typical squamous cell epithelioma and should be excised widely. There is no need for a preliminary specimen for biopsy in a frank case of this kind.

DR S. W. BECKER: For years I have been performing biopsies on small lesions. This lesion has the semiglobular shape of an early squamous cell epithelioma. This man is a machinist and insists that he hurt the finger. No one could work in a machine shop without knocking his knuckles, hence he has surely had multiple traumas. On the other hand, I have had women and men with such lesions on the face, where there has been no trauma. I do not believe that trauma can be called the chief factor in the production of this lesion.

DR FRANCIS W. LYNCH, St. Paul: The question of the relation between trauma and cancer is one that deserves special consideration by those who are called before industrial commissions and the courts. There is an interesting and thorough discussion of the problem by Berenblum, a member of the Oxford Commission on Cancer (*Arch. Path.* 38:233 [Oct.] 1944). It is an excellent discussion, which should be read by all who are interested in the problem.

DR MAURICE OPPENHEIM (by invitation): I think that this is a case in which the diagnosis can be made only by biopsy. As Dr. Becker said, the lesion looks like cancer. It came on two months after injury. It is exceptional that a traumatic cancer originates from a normal skin. In most cases the real traumatic cancer develops on a base of a scar or on skin changed otherwise.

DR S. W. BECKER: I have been astounded at the rapidity of growth in many of these tumors. I have one man who has been working with oil whom I have been treating for two or three years. Five or six of these growths have developed on the face and neck. He comes in with a typical squamous cell tumor, with a history that it has been present only two or three weeks.

DR CLEVELAND WHITE: The interesting feature was the history of trauma. Of course, an absolute diagnosis cannot be made without a biopsy, but I feel as Dr. Montgomery does that it is a squamous cell epithelioma.

At the meeting last month Dr. Weber discussed the question of cancer due to trauma. Such cases are being encountered more frequently, and it has come to the point where one must try to determine whether or not trauma can clinically cause cancer. In the past three years I have seen a few cases of epithelioma in which trauma has allegedly been a factor. The physician who cared for this man at the time of the injury said that the wound healed rapidly and completely and that there was no sign of a growth until several weeks later. As Dr. Becker said, epithelioma can develop in a short time. As far as oil is concerned, I do not believe that a diagnosis of cancer due to oil can be made, because there is no folliculitis or comedos of any type. It is planned to have the lesion excised completely.

NOTE.—The tumor was excised completely by a surgeon and reported by the pathologist to be a grade I squamous cell epithelioma, with portions resembling pseudoepitheliomatous proliferation.

DR STEPHAN EPSTLIN, Marshfield, Wis. I agree with Dr Becker and Dr White that this is a typical squamous cell epithelioma. Ewing listed six essential criteria in determining the probable relation of trauma to tumors: (1) the authenticity and adequacy of the trauma, (2) the previous integrity of the wounded part, (3) a reasonable time relation, from three weeks to three years or more in certain cases, (4) continuity of symptoms of the injury with those of the tumor, (5) microscopic or other proof of existence and histologic type of a tumor, and (6) the location of the tumor at the point of injury.

The problem of trauma and cancer has interested me for a number of years. I have seen a fairly large number of cancers of the skin. One gets a history of trauma not infrequently—usually minor everyday traumas that do not appear significant. I found, however, that in those rare instances in which cancer of the skin originates before the age of 30, histories of definite well attested injuries are frequently volunteered. From these observations I am convinced that a single trauma can produce cancer.

**Giant Nevus Pigmentosus and Verrucosus of the Thigh Treated by Complete Excision and Primary Grafting** Presented by DR S J ZAKON and (by invitation) DR J T GAULT

A G, a white man aged 40, was first seen on July 6, 1944. The examination revealed the presence of a pigmented verrucous hairy nevus, dark brown to black, involving the inner aspect of the left thigh and leg extending from the upper half of the thigh to the upper third of the leg. The nevus measured 12 inches (30 cm) in length and 8 inches (20 cm) in width and presented numerous fissures, most of which were secondarily infected and exuded a foul odor. At the bend of the knee there was a tender swollen eroded bleeding node. The patient's general condition was good. Biopsy of this painful lesion revealed an active melanotic nevus.

On July 28, after careful preoperative preparation, the entire nevus was excised with more than  $\frac{1}{4}$  to  $\frac{1}{2}$  inch (0.64 to 1.27 cm) margin of normal skin. The excision extended down to the subcutaneous tissues. The excised area was covered with sterile strips of petrolatum gauze and a pressure bandage was applied. On August 18, a full thickness skin graft was cut from the donor areas with a Padgett dermatome. The sheets of skin were placed on the defect and were sutured to one another and to the periphery. The grafts healed by first intention, and the patient was sent home on September 10.

DISCUSSION

DR H E MICHESON, Minneapolis. I believe that dermatologists have finally learned that this type of lesion should be treated by surgical excision first and not last. I think that it is a great mistake for any other type of treatment to be tried before excision is used. A certain percentage of these large nevi do become malignant, and removal is the best prophylaxis.

**Favus in an American-Born Family** Presented by DR MICHAEL H EBERT

R P, a white boy aged 13, presents an eruption of the scalp, which he states has been present for two years. His sisters, aged 14 and 19, have the same eruption. They were all born and reared in Chicago. About 80 per cent of the scalp is involved, and the crown is almost bald. There are a few coin-sized irregular atrophic areas. The rest of the scalp is covered with a lemon yellow adherent crust with a mousy odor. There are many typical cup-shaped scutula. Typical hyphae were demonstrated in the scutulum.

DISCUSSION

DR RUBEN NOMLAND, Iowa City. This is the third family I have seen in Chicago in which the third generation had favus.

DR I M FELSHER. In the cases we had a few years ago there was a yellowish fluorescence under the Wood light.

**Rhino-sporidio** is presented by Dr. OLIVER S. OLIVER and (by invitation) Dr. L. V. L. BROWN.

C. J. Mc... a woman aged 26, was first seen by us, five weeks ago. There was a small tumor situated on the conjunctiva in the inner corner of the right eye, which had been present for six months. The lesion was the size of a small coffee bean and oval in contour. The color was purplish red and the surface was covered with minute white spots. There were no subjective symptoms, but there was some increased lacrimation. One treatment with roentgen rays was given on the first examination which had little effect on the tumor.

Dr. OLIVER S. OLIVER: I saw the patient several weeks ago, and I had no idea as to the diagnosis. I had not seen anything like it as a therapeutic test. I saw her one treatment with roentgen rays which reduced the tumor somewhat. The book on clinical mycology prepared by Dr. Cullen and other somewhat recently received, presented an illustration of an identical lesion which was recognized by Dr. Albert (Conant, N. J., and other. *Manual of Clinical Mycology*, prepared under the auspices of the Division of Medical Science of the National Research Council, Philadelphia, W. B. Saunders Company, 1944, p. 200). The examination for the parasite to be done is one which could examine for other spores with potassium hydroxide. The organism cannot be grown, hence nothing can be proved by bacteriologic examination. I take it that examination of the material in the culture is not hard to demonstrate. We are going to demonstrate the spores as soon as possible.

This disease occurs in the tropics, and one of the lesions are extensive and in some areas become large masses. In one case the disease is serious. The cases in which the eye are involved are chiefly the description of these cases as given in the aforementioned book is exactly as seen here—a small nodule or tumor, bluish red, with white bodies on its surface. It is the white bodies that contain the material in which the microorganism are found.

**Poracea-Jake Tuberculid of Lewandowski** presented by Dr. S. ROBINSON and (by invitation) Dr. A. J. SATANHO.

J. O., a white woman aged 32, was first treated in the University of Chicago Clinic in 1936, for acne vulgaris. After a lapse of three years she returned, in 1939, with a facial eruption which was diagnosed clinically and histologically as to acne-like tuberculid of Lewandowski. For the next nine months she was treated with local ultraviolet irradiations given with the water-cooled quartz mercury vapor arc lamp, and she received twenty intravenous injections of gold immunum succinylate in graduated doses of from 25 to 500 mg, with some improvement.

In August 1944, the patient again returned, because of an exacerbation of the eruption. She presented small red papules spread densely over both cheeks and forehead. On diascopic pressure yellowish brown spots remained at the site of the papules. The nose, perioral region, center of the chin and side surfaces of the forehead were completely free. Treatment similar to that which she received four years previously was instituted, and decided improvement has been noted. A biopsy section is presented. It shows massive infiltrate, consisting of round cells, epithelioid cells and giant cells, extending rather deeply into the corium. Roentgenograms of the chest have never been found. Old tuberculin in a 1:10,000 dilution elicited a negative reaction and in a 1:1,000 dilution a positive reaction. The Wassermann and Kahn reactions of the blood were negative. The blood count was normal, except for a transitory leukopenia during the course of the reaction. The patient has been pregnant three times. The first pregnancy resulted in an anencephalic stillborn baby, the second terminated in the birth of a 6 month

premature baby which died, the third resulted in a normal baby, delivered by cesarean section because of a placenta previa

#### DISCUSSION

DR H E MICHELSON, Minneapolis I wish I were able to crystallize an opinion on this condition, but all I can do is to give you my convictions in the matter Dr Laymon and I prefer the name "maculopapular tuberculid" in preference to "rosacea-like tuberculid" We have voiced our objections to the latter term before We think that the clinical criteria are that the papules are small, are not necrotic, have a dark red color and do not coalesce and that the microscopic observations closely simulate those found in sarcoid In our experience the course is extremely variable Some patients get well without treatment in a short time, others do not respond to any treatment, but later the lesions do disappear Some of the patients react positively to tuberculin, and some do not Unfortunately, the bacilli cannot be found, although the presence of tuberculosis has been demonstrated in a fairly large percentage of the patients Dr Miescher not long ago reviewed a series of these cases, and he felt that in frank rosacea there was a similar microscopic picture at times This we have been unable to corroborate I believe that there are some papular rosaceas that look just like this eruption but are not tuberculous, and I do not believe that when an antirosacea regimen does not bring about a cure the disease is therefore tuberculosis We are convinced that the diagnosis of rosacea-like tuberculid is made much too often

DR HAMILTON MONTGOMERY, Rochester, Minn The histologic sections in this case show typical tubercles and not just a few collections of epithelioid cells I agree with Dr Michelson that one sees collections of epithelioid cells in cases of diseases that have been diagnosed as various forms of tuberculids but which more probably were rosacea not tuberculids In the present case, however, the histologic structure is definitely that of tuberculosis

DR OLIVER S ORMSBY I should like to make a therapeutic suggestion, which I rather dislike to do in view of the fact that treatment is considered ineffectual by many I have shown to this society a patient with generalized sarcoid that was cleared with ethyl chaulmoograte Because of the good results secured also in 2 cases of rosacea-like tuberculid, I suggest its use for patients that have resisted other methods of treatment

DR C W LAYMON, Minneapolis, Minn I merely want to say a word about sensitivity to tuberculin in these cases Some observers have stressed the importance of a high degree of sensitivity in this type of tuberculid in contrast to a much lower degree of sensitivity in tuberculosis miliaris disseminata, for example In the cases of so-called rosacea-like tuberculid which we have studied at the University of Minnesota there has been such a tremendous variation in the reactions to tuberculin that it has been of little importance diagnostically

DR S ROTHMAN I am grateful for Dr Ormsby's therapeutic suggestion and will gladly follow it

I agree with Dr Michelson that "rosacea-like" is not a fortunate adjective But I object even more to the term "tuberculid" In modern dermatology I believe that the term "tuberculid" should be restricted to eruptions which are due to a shower of tubercle bacilli embolizing in the skin in persons with an extremely high degree of tuberculous allergy Owing to this allergy the embolizing tubercle bacilli are more or less rapidly and more or less completely destroyed in the skin Therefore, animal inoculation and histologic demonstration of bacilli in lesions of tuberculids is rarely successful, and histologically one finds all transitions between banal inflammatory infiltrates and classic tuberculous structure, obviously dependent on the speed with which tubercle bacilli are decomposed According to this definition three diseases can be called tuberculids lichen scrofulosus, papulo-necrotic tuberculid, including the follicular-papular forms, and erythema induratum of Bazin In all these diseases one finds strong reactions to tuberculin in dilutions

of 1 1,000,000 or at least 1 100,000 and one can safely assume that the patient harbors living tubercle bacilli somewhere in his body. This is not the case with sarcoidosis, tuberculosis miliaris disseminata faciei and Lewandowski's disease. The last two diseases display tuberculous or tuberculoid structure histologically, but there is no definite evidence that they are due to tuberculous bacillus and the clinical course must be the local action of a greatly mitigated bacillus, because the sensitivity to tuberculin is of a conspicuously low degree—in any case never as high as in tuberculids. This patient's reaction to tuberculin, for instance, is negative to old tuberculin in a dilution of 1 10,000 and only weakly positive to old tuberculin in a dilution of 1 1,000, this is the average reaction of a city dweller. The clinical significance of a sharp separation of these diseases from "tuberculids" is obvious. In tuberculids one has to search for active tuberculous lesions, because the presence of tuberculids means activity, whereas tuberculosis miliaris disseminata faciei and Lewandowski's disease do not mean that. Therefore, I am sorry that I cannot agree with Dr Laymon. I believe that the thorough quantitative study of sensitivity to tuberculin in all these diseases contributes a great deal to one's understanding of the pathogenesis of cutaneous tuberculosis and is clinically highly important.

**A Case for Diagnosis (Periarteritis Nodosa?)** Presented (by invitation) by  
CAPT LESTER W. KIMBERLY, MC, AUS

M J S, a white man aged 25, first noticed small tender nonpainful nodules on the flexor surface of the right forearm in October 1942. About seven months later he noted similar nodules on the left side of the abdomen and also that the nodules on the right forearm were disappearing leaving a mottled reticulated bluish network outlining the pattern of the blood vessels in the skin or subcutaneous tissue. Since then new nodules have continued to appear about the waist, on the lower part of the abdomen, in the crural area on the thighs, in the right popliteal space and on the chest, back, arms, forearms, palms and soles. They vary from a few millimeters to 15 cm in diameter, and are firm, discrete and movable. Most of them have receded, leaving the reticulated pattern now seen.

The Kahn reaction of the blood was negative, as was that of the spinal fluid. The urine and blood were normal. The results of gastric analysis were within normal limits. The sedimentation rate was 10 mm in one hour. The values for blood chemistry were within normal limits. The roentgenograms of both legs and both forearms revealed no changes of soft tissues or bones, those of the heart and lungs showed no abnormalities.

Histologic examination of a late lesion showed no essential change in the epithelial hair, sebaceous glands and sweat glands. At the junction of the dermis with the subcutaneous tissue there was an area of chronic inflammatory reaction characterized by an infiltration of lymphocytes, plasma cells, eosinophils and macrophages and some areas containing polymorphonuclear leukocytes. The infiltration of inflammatory cells involved the fibrous tissue. The perivascular spaces were also involved, these were more striking at the margins of the lesions. The inflammatory cells were primarily of the mononuclear type previously mentioned. There was a thickening and increased cellularity of the smaller vessels, many appearing to be almost solid cords. The adventitia about some of the larger vessels was edematous, containing chiefly lymphocytes and plasma cells. Occasionally there were a few inflammatory cells within the larger arterial walls. The histologic changes of the lesion were considered nonspecific.

DISCUSSION

DR C W LAYMON, Minneapolis. This to me was one of the most interesting cases of the day. In most cases unfortunately, the diagnosis is made post mortem by the pathologist. The mortality is high, and males are affected much more frequently than females. The kidney, heart and liver are involved much oftener

than the skin. Reddish or purplish brown reticular lesions such as were seen in this case are suggestive of a relatively benign or chronic type of periarteritis nodosa.

DR RUBEN NOMLAND, Iowa City. The experience at the University of Iowa is that the cases of periarteritis nodosa that come to necropsy have mostly been from the neurologic service, because the patients had had neurologic symptoms as their chief complaint. One of the conditions that the pathologist at the University Hospital has been able to demonstrate is an involvement of the peripheral nerves. The sections show a chronic inflammation about a medium-sized nerve.

DR MAURICE OPIENHIEM (by invitation). The nodules in this case looked like those of periarteritis nodosa. There are definite infiltration and nodulation. In my department of dermatology in Vienna I gave such a case the name of "apoplexia cutanea," because a sudden deep hemorrhage of the skin originated. The patient a woman, died suddenly during my rounds, and histologic examination showed periarteritis nodosa of the skin and of the internal organs. With regard to the skin the foci were located around the bifurcation of the arteries in the subcutaneous tissue. The case was published by my assistant Dr. Freund in the German *Archiv für Dermatologie und Syphilis*. I believe, as does Dr. Laymon, that this is one of the exceptionally rare cases of periarteritis nodosa of the skin.

DR ARTHUR C. CURTIS, Ann Arbor, Mich. (by invitation). I was glad to see this case for two reasons. I have seen several cases of periarteritis nodosa that have been diagnosed ante mortem, but this is the first case in which there has been an erythematous eruption or, for that matter, an eruption of any type. Second, the patients I have seen have not had the characteristic nodules along the vessels. One would think that this would be a common finding, but too often many patients are seen before nodulation occurs. The pathologists see nodules often, the clinicians seldom. This patient has the most striking nodules along the brachial artery that I have ever seen.

Periarteritis nodosa is a disease that has several stages. It often begins like an infection, and frequently bronchial asthma, urticaria or erythema multiforme is present. In the acute stage, a high fever, leukocytosis and eosinophilia with a count of 30, 40 or 70 per cent may be present. As the disease progresses, and if the patient does not die, a chronic state is reached, which is represented by this patient. The leukocyte count is normal, and the eosinophils have fallen to a normal of 2 per cent. He has no manifestations of activity of his disease, except fatigue and a history of loss of weight.

Dr. Rich, at St. Louis, has produced in animals a pathologic picture identical with periarteritis nodosa by inducing in them sensitivity to injected horse serum and then giving large doses of this protein parenterally.

DR PAUL O'LEARY, Rochester, Minn. My concept of periarteritis nodosa is similar to that of Dr. Nomland in that sensory changes in the skin are commoner than are the dermatologic ones. In fact, the cutaneous picture is so varied that it has been quite impossible up to date to describe the classic cutaneous picture of this syndrome.

Several years ago a patient with anesthetic areas about the face, especially about the mouth, and about the arms and chest, with associated pigmentary changes in these areas, was found to have acid-fast bacilli in the smear of nasal material. These organisms were similar to Hansen's bacilli and were accepted as such by the laboratory at Carville, La. The patient died shortly thereafter, after an acute flare-up of a previously recognized nephritis, and at autopsy a diagnosis of periarteritis nodosa was made and no evidence of leprosy was demonstrated.

I have had a similar experience in which acid-fast organisms were demonstrated in a similar case, and, while I do not for a moment infer that this patient has leprosy, I hope that Captain Kimberly will have the opportunity to examine a smear of nasal material for acid-fast organisms.

DR S. W. BECKER. I was much impressed by the vascular changes. I thought of livedo racemosa of Ehrmann. I stroked the skin in order to express the blood from these areas, and the blood returned somewhat slowly, but it returned as

venous blood, which identifies the disease as an obliterative one. Ehrmann's patients usually had tuberculosis or syphilis. This man's disease is evidently a more acute affair, but the vascular change is evidently similar to, if not the same as, that in Ehrmann's livedo racemosa.

CAPT LESTER W. KIMBERRY, M.C., A.U.S. (by invitation) I presented this case in the hope that I might get some therapeutic suggestions. I had never seen anything like it before.

NOTE.—The patient was subsequently given 1,200,000 units of penicillin, without any effect on the development of new lesions.

**Idiopathic Multiple Pigmented Sarcoma (Kaposi?)** Presented (by invitation) by DR. MAURICE OPPENHEIM

L. O., a white man aged 42, presents on both soles on the lateral parts of both feet and over the ankles symmetric bluish red spots and infiltrated plaques with a smooth surface. The macules vary in size from that of an almond to almost diffuse involvement of the soles. The margins are sharp. Diascopy revealed a yellow-brown color. There are no erosions or ulcerations. On several toes of the left foot there are pinhead-sized nodules, sharply limited, of dark blue color and hard consistency, like warts. On both legs there are sharply limited round depressed pigmented scars the size of a dime.

The disease began seven years ago in Italy without subjective symptoms. The patient has diabetes, but the urine is now free of sugar, and the blood sugar level is 130 mg. per hundred cubic centimeters. He is on a diet for diabetic patients. He was never treated by a dermatologist. He is now taking solution of potassium arsenite, U.S.P., and Grenz rays are to be used.

The urine was normal except for a faint trace of acetone. The blood count was normal. The differential count showed 4 per cent eosinophils. The blood cholesterol level was 143 mg. per hundred cubic centimeters.

A section from a diffusely infiltrated area of the ankle was removed for histologic study, with the following results. The epidermis was normal, the papillary layer was partially flattened. There were many newly formed capillaries, partially enlarged and partially closed by a growth of endothelial cells. At some places there were formations resembling angiomas. There was necrosis of the connective tissue in the neighborhood of the capillaries. Lymphocytic elements and a few mast cells and plasma cells were present. There were many enlarged lymphatic vessels. There were no hemorrhages but hemosiderin, mostly extracellular, was present in all parts of the tissue. The connective tissue was acidophilic and poor in fibrocytes. In some areas the sweat glands were cystic and hypertrophic.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn. I believe that this is a case of Kaposi's sarcoma. The histologic changes are not so typical as one usually sees. There are no sarcomatous changes or collections of lymphocytoid cells. There is proliferation of the walls of the capillaries, resembling in some respects the early phases of hemangioendothelioma. Some French authors regard Kaposi's sarcoma as a hemangioendothelioma. The sections also show definite disposition of pigment, and if stains for iron were made would, I believe, reveal the pigment to be hemosiderin and not melanin. The histologic picture in this case would explain and fit in with the long duration of the process.

DR. DAVID LILBERTHAL. The most interesting point in this case is that the disease remained stationary for years without the patient's having received any treatment during the time. In this disease one sees progressive development in the spread and the clinical changes and after a few years a fatal termination.

DR. MAURICE OPPENHEIM (by invitation). Clinically, there is no doubt that it is Kaposi's sarcoma. The infiltration, the purplish color, the location of the pigmented scars on the legs, the symmetry and other aspects are typical. As Dr.



Lieberthal says, it shows a chronic course. Such cases are known to occur. But more interesting are the histologic observations. As I saw the histologic structure, I thought first of hemangioendothelioma tuberosum multiplex because there are many newly formed capillaries, sharply limited against the enlarged tissue. There are many enlarged lymphatic vessels, and the connective tissue is almost unchanged. It looks like the third stage, the so-called angiomatous stage, of the disease. There were no spindle cells in the tissue. This is remarkable in a case of pigmented sarcoma of Kaposi, especially in such a chronic case. All through the section hemosiderin was present in large amount, hence there is no doubt that many hemorrhages took place.

As Dr Lieberthal says, this case should be studied. There was only 130 mg of sugar per hundred cubic centimeters of blood. It is possible that this disease has something to do with the diabetes, but the cholesterol level is only 143 mg per hundred cubic centimeters, hence I am a little doubtful that the case should be diagnosed as a true case of Kaposi's sarcoma. Clinically it is, but histologically it is not so certain.

DR HAMILTON MONTGOMERY, Rochester, Minn. There are cases of Kaposi's sarcoma described in the literature with histopathologic changes similar to those seen in this case.

DR MAURICE OPPENHEIM (by invitation). In Gans's "Histology of Skin Diseases" there is a picture of Kaposi's sarcoma which is similar to the histopathologic changes in my case. Ordinarily one would hesitate a little to consider these cases as instances of Kaposi's sarcoma.

**Pemphigus Erythematosus(?)** Presented by DR HERBERT RATTNER and DR THEODORE CORNBLEET and (by invitation) DR M S KAGEN

A 63 year old white man of Polish extraction had thick greasy scales on the scalp at the age of 40. Seven weeks ago yellowish scales appeared on the alae of the nose, followed by blisters on the hands, chest, back, face, legs and forearms. The patient has improved with treatment consisting of potassium permanganate baths, 1 per cent gentian violet medicinal, dusting powders, 40 per cent sulfur paste and acetarsone and sulfadiazine administered orally.

#### DISCUSSION

DR FRANCIS E SENEAR. I felt that this was not pemphigus erythematosus but rather a true pemphigus vulgaris. The lesions on the scalp have been present for some time and may be looked on as the primary lesions which Dr Oppenheim has written about and talked about. The generalized eruption is of only seven weeks' duration. I have seen 2 cases of pemphigus erythematosus in which that typical picture had existed for some time, and subsequently there developed a bullous eruption typical of pemphigus vulgaris. I have never seen that happen with the rapidity that has taken place in this case, however. Furthermore, the lesions on the alae nasi seem to be vegetative ones, such as are seen in pemphigus, but not the lupus-erythematosus-like lesion seen in the more benign type of the disease.

DR THEODORE CORNBLEET. I naturally had in mind the various members of the bullous group, particularly erythema multiforme and pemphigus. The exact placement in the pemphigus group, if this is pemphigus, we were not certain about, but the rapidity and the greatness of the changes that can occur in the eruption in the erythematous type of pemphigus should make one think of this as a label for this patient's disorder. This may be the correct diagnosis, but a definite one had perhaps better wait for the future.

**Adiponecrosis Subcutanea Neonatorum** Presented by DR DAVID V OMENS and (by invitation) DR HAROLD D OMENS and DR M S KAGEN

W G, a Negro boy aged 5 weeks, presents a hardness of the skin of the back involving almost the entire back and extremities, especially the lateral aspects

This hardness appeared three days after birth in localized areas which spread and coalesced to the present involvement.

On Dec 10, 1944, the mother, a 28 year old Negro woman, was brought into the hospital in the early part of the last month of her pregnancy, with a temperature of 103 F. It was decided to induce labor, which was done by rupturing the membranes. The labor was short and not difficult, the baby being born with head presentation. During labor the mother was given sedatives (Stroganoff's method). On delivery the child was cyanotic and subsequently showed repeated manifestations of cyanosis with conjunctival hemorrhages. Because its condition gradually became worse, on the third day the child was removed to the Children's Hospital, where the cutaneous manifestations began to appear and were accompanied with a fluctuating temperature ranging from 100 to 103 F, with abscesses which on culture showed *Staphylococcus aureus*. Culture of the blood yielded the same organism. The Kahn reaction of the mother's blood was negative. The child has been given sulfonamide compounds, and for the past three days the temperature has been normal and he is showing improvement in health.

The histologic examination of a specimen removed showed a mild acanthosis of the epithelium, edema of the collagenous tissue of the entire cutis, dilatation of the lymph and blood vessels and an increase in the connective tissue cells. The appendages of the skin participated in the edematous process. In the junction of the cutis and the subcutaneous fat there was an infiltrate composed of small lymphocytes, plasma cells, histiocytes and fibrocytes which tended to involve the trabeculae of the fat cells, which were thickened and contained a homogeneous substance like a coagulum.

#### DISCUSSION

DR C W LAYMON, Minneapolis. A diagnosis of necrosis of subcutaneous fat should be strongly considered in this case. The disease appears from a few days to three weeks after birth and disappears spontaneously within a few months. The locations of the lesions in this case were characteristic, being on the back, buttocks and extremities. True sclerema neonatorum occurs within the first few days of life in debilitated babies and is almost always fatal within a short time. The involved skin is firm and shrunken and cannot be lifted in folds as in this case.

DR S ROTHMAN. Sclerema neonatorum represents a diffuse solidification of the subcutaneous fat tissue due to a pathologic shift in the composition of the fat. The body temperature is subnormal, and the babies die in a few days. The circumscribed hard cutaneous-subcutaneous nodes with slight erythema on the surface in the presented case correspond with what was described as adiponecrosis subcutanea neonatorum. It is probably due to injuries received during delivery, and its prognosis is absolutely favorable.

DR DAVID V OMFES. In answer to Dr Laymon, I would say that the area he felt was the uninvolved area. In the areas that were definitely involved he would have found it difficult to raise the skin from the underlying tissues. There was a grayish color to the cut surface of the subcutaneous tissue. The patient has what I thought were the characteristic features that were primarily described by Dr Gray, of London, England, twenty years ago.

The histologic section presented what looked like a coagulum of the fatty tissue. The fat cells were filled with a protoplasmic substance which took origin from the fat cell membrane or trabeculae, with a lymphocytic cellular infiltrate above the surface of the fatty tissue extending down to involve the trabeculae, and there was no evidence of necrosis in the entire section.

#### Seborrheic Dermatitis with a Decided Palpebral Involvement Presented by DR MICHAEL H EBERT

P B, a white man aged 28, presents a decided inflammation on the margins of the eyelids and an eruption in the bearded region. He states that the lids have been involved since he was 2 years old and that he has had many types of treatment in hospitals for diseases of the eye, including surgical removal of the margins.

of the lower lids. In May 1943, redness and scaling appeared in the bearded region, which were cleared in 1944 by roentgen ray therapy. After three months the eruption recurred and persisted. There is ectropion of the lower lids, with an operative scar along the palpebral borders. The palpebral conjunctiva is granulomatous. There is a mild blepharitis of the upper lids. The bearded region is dull, red and scaly.

## DISCUSSION

DR THEODORE CORNBLEET: May I suggest the possibility of sycosis barbae for consideration? The eyelashes are involved, something that I have seen happen before in this disease.

DR MICHAEL H. EBERT: Dr Cornbleet's point is well taken. When we saw this man for the first time, on January 8, he was in rather poor condition. He had a long beard, his hair was shaggy, and he was dirty. When the beard was clipped the eruption appeared. When I saw him again, there were a diffuse infiltration and redness but no pustules. Yesterday there were no pustules, but today there are definite follicular pustules. I accept the diagnosis of sycosis barbae with secondary dermatitis of the bearded region and involvement of the eyelashes. The extraordinary thing in this case is the early onset. I think that the involvement of the lashes is due to the same type of staphylococcus that lives on the skin.

**Ainhum.** Presented by DR DAVID V. OMENS and (by invitation) by DR HAROLD D. OMENS and DR M. S. KAGEN.

L. S., a Negro butcher aged 39, complains of pain in the small toe of the left foot which is severe on excessive walking and at night when resting.

On examination there is a constricting ring just below the first phalanx encircling the entire toe and producing a bulbous distention of the distal portion of the toe. A roentgenogram revealed no osseous involvement but just a constricting ring of the soft tissues. The report on the Wassermann test has not been returned.

This patient has lived in Chicago for the past twenty-seven years, previous to that time he lived in New Orleans. He said that he has not walked barefooted and has had no injury to his feet at any time, however, he stated that on that particular toe he had a corn which is not present now.

## DISCUSSION

There was no discussion of this case.

**A Case for Diagnosis (Squamous Cell Epithelioma?)** Presented by DR MICHAEL H. EBERT and (by invitation) DR M. S. KAGEN.

M. G., a Negro woman aged 25, presents an ulcerated area, 5 cm. in diameter, to the left of the anus. A "boil" appeared in this area eleven months ago, and a similar one appeared on the opposing surface of the right nates. The one on the right disappeared in a few weeks, but the one on the left persisted and ulcerated. The ulcer was so tender it interfered with walking. She has congenital syphilis and had intermittent treatment until 1941. The Wassermann reaction of the blood serum is positive at the present time. The Frei test elicited a negative reaction. Since the patient received a course of sulfathiazole the ulcer has cleared and is much less tender. At present there is an irregularly outlined ulcer 5 cm. in diameter. The floor is granulomatous, with a few persistent islands of epidermis. The border is level with the surrounding skin and not undermined. The base is moderately infiltrated.

## DISCUSSION

DR LOUIS H. WINER, Minneapolis: The histologic section was spread all over the slide. I showed it to Dr S. W. Becker, and he agreed with me that there was an island which showed epidermal proliferation much in the manner of a squamous cell epithelioma, hence, I offer that as a diagnosis.

DR MICHAEL H. EBERT: The section was taken from the inner margin near the active ulcer, but the tissue was so friable that the pathologist could do no

better with the slide. I thought that there was more epithelial proliferation than one sees in pseudocarcinomatous changes in marginal ulcers, and from the histologic appearance I was almost inclined to think that it was an epithelioma.

## PHILADELPHIA DERMATOLOGICAL SOCIETY

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Jan 19, 1945

A Case for Diagnosis Presented by DR. THOMAS BUTTERWORTH, Reading, Pa.

T. S. R., a white man aged 35, a robust steel worker, presents a raised, annular, circinate, serpiginous and flesh-colored eruption involving the back and posterolateral aspects of the neck. The eruption had its onset about Nov. 1, 1943, it has improved at times but never entirely healed.

The serologic tests of the blood for syphilis elicited were negative reactions. The urine was normal. The biopsy specimen was reported as characteristic of atypical lupus erythematosus, conceivably with a tuberculous base.

The patient was given 900 r of roentgen rays in divided doses to selected lesions, without effect. Bismuth subsalicylate in oil, 1.25 cc of a 13 per cent suspension, was administered weekly for eight weeks. Various keratolytic ointments were without value.

## DISCUSSION

DR. SIGMUND S. GREENBAUM: The histologist did not make a diagnosis, hence at least the provisional diagnosis will have to be made clinically, which happens not infrequently.

DR. MORRIS MARKOWITZ: Histologic examination shows a few things—for instance, numerous fibroblasts and basophilic degeneration—which occur frequently in granuloma annulare. However, it could also be a tuberculous disease.

DR. SIGMUND S. GREENBAUM: I do not think that it is lupus erythematosus clinically. I think that it is closer to granuloma annulare or to a type of serpiginous sarcoid than it is to anything else. It would be interesting to see the effects of irradiation on one of those annular lesions on the left side of the neck and of arsenic taken by mouth. This patient should be presented again in thirty or sixty days.

DR. MORRIS MARKOWITZ: Why not destroy one half or one third of the lesion by electrocoagulation? It sometimes happens that when one lesion is destroyed by electrocoagulation the others disappear spontaneously.

DR. HERMAN BEERMAN: This histologic section is so well made and so clear that all the features which Dr. Weidman has on his protocol are easily observed independently by any one looking at it. I cannot see anything there to suggest granuloma annulare. In fact, the striking thing is the fact that it looks more like lupus erythematosus, and then when one looks at it closely it does not. I think from reading Dr. Weidman's note that he had the same opinion.

DR. MORRIS MARKOWITZ: Basophilic degeneration and fibroblasts occur in granuloma annulare.

DR. HERMAN BEERMAN: Basophilic degeneration is seen in warts, too.

DR. JOHN F. WILSON: Has the eruption always looked the same?

DR. THOMAS BUTTERWORTH, Reading, Pa.: Approximately the same. At times it gets better and then reverts to the form seen tonight. I do not want to electrodesiccate any of the lesions, because they disappear without any scarring. I do not want to do anything poorer than Nature is doing.

DR. CARMELYN C. THOMAS: Have you tried to exclude light from the lesions?

DR THOMAS BUTTERWORTH, Reading, Pa On what grounds?

DR CARMEN C THOMAS On general principles I do not know the nature of the patient's work Is he exposed to arc lights?

DR SIGMUND S GREENBAUM Each of those lesions has an unusual filiform infiltrated border, and Dr Corson presented a case like this years ago, which was pictured in the textbooks as a circinoid type of sarcoid If the histologic conditions definitely exclude granuloma annulare, I think this is the only other condition to think of, clinically

DR HERMAN BEERMAN It does not look like that, either, histologically

DR SIGMUND S GREENBAUM Well, a good many of the histologic diagnoses do not agree with what one sees clinically Many times one cannot make the diagnosis on histologic grounds

DR MEYER L NIEDELMAN Was the biopsy specimen taken from one of the older lesions?

DR THOMAS BUTTERWORTH, Reading Pa One cannot say that one lesion is older or younger The whole process is in a state of flux

DR SIGMUND S GREENBAUM I would use solution of potassium arsenite U S P Kissmayer thinks that all lesions clear up with arsenic

#### Familial Lentigines Presented by DR MORRIS MARKOWITZ

The McC family presents a family group of three brothers and three sisters and a father The mother, who is dark-haired, is not affected The patients are red-headed, except for a dark-haired 9 year old boy and a blond 19 year old girl The ages of the children range from 7 to 19 years The lesions had been noticed soon after birth, and their characteristics remained unchanged in all seasons (they are not affected by sunlight) They are symmetrically located on the face, shoulders and upper part of the back, appearing as round noncoalescent macules, of a yellow color and ranging from a pinhead to a pea in size

Determinations of the blood chemistry of the 2 boys, aged 7 to 9 years, showed cholesterol, 200 to 220 mg, calcium, 10 to 15 mg, sugar, 100 to 120 mg, and urea nitrogen, 9 to 20 mg, per hundred cubic centimeters of blood

#### DISCUSSION

DR THOMAS BUTTERWORTH, Reading, Pa I think that is the common combination in the Irish—red hair and freckles

DR MORRIS MARKOWITZ Should one call that simply freckles, or should one make a distinction between freckles and lentigines? I think that I should make a distinction

DR SIGMUND S GREENBAUM Of course the French and, I think, the Germans differentiate lentigines and freckles These patients have freckles The boys have them on the face and on the shoulders Sometimes the differentiation between lentigines and freckles is not easy I saw a patient only today with hundreds of pigmented lesions on the shoulders and face, developing after exposure to sunlight While it is often difficult to differentiate lentigines and freckles, I think that in this case it can be done Lentigines, by the French and, I think, by Ormsby, are placed in the group of pigmented nevi developing late in life and sometimes under the influence of chemical rays or sunlight or roentgen rays These patients have freckles, not lentigines

DR MORRIS MARKOWITZ Another thing one would not think of with regard to freckles is that they are not changed by exposure to light but sometimes become more prominent in the dark These occurred soon after birth Usually freckles appear when the child is 5 or 6 years old

DR JOHN F WILSON The shoulder strap regions are less involved, and the "V" of the neck is fairly sharply margined

DR SIGMUND S GREENBAUM Yes, the sunlight brings the freckles out I think that some one makes the distinction that the melanin is deep down in the basal cell layer in lentigo

**Nevus Pigmentosus Lateralis** Presented by DR REUBEN FRIEDMAN

K F, a white boy aged 7 years, presents numerous areas of light brownish hyperpigmentation confined to the left side of the chest, the left arm and the left side of the back and neck One brownish streak, about 0.5 to 1 cm wide, extends from the middle of the extensor surface of the left forearm up along the inner aspect of the arm and across the left shoulder, terminating behind the acromion process Two shorter linear parallel processes are noted on the posterior aspect of the left arm A large irregular patch on the left side of the back extends upward along the vertebral column from the fifth lumbar vertebra, gradually fanning outward and upward and then curving across the upper part of the back to the neck and shoulder Another patch is located on the chest, extending from the middle of the manubrium sterni to the shoulder There have recently developed two small patches of faint hyperpigmentation in the right portion of the epigastric region and at the right costal margin

The Wassermann reaction of the blood was negative

Shortly after the patient's birth his mother noted a small, thin, linear area of hyperpigmentation about  $\frac{1}{4}$  inch (0.64 cm) long, on the middle of the outer side of the left arm It remained stationary for a year and then began to spread from that point both upward and downward in linear fashion New similar patches have developed from time to time

DISCUSSION

DR SIGMUND S GREENBAUM Another interesting thing about this case is that the youngster has three new café-au-lait pigmented spots developing on the chest, one anteriorly and two posteriorly He is sure that they are new ones, and I agree with him This eruption was small in the beginning but has increased from time to time I think that one ought to consider not only a simple condition of unilateral pigmented nevus but the condition described by Bloch and Sulzberger There is not an increase of melanin or an increased dopa reaction, but an absence of real nevus cells, hence a biopsy, if possible, might be of interest for a later report. It is not an out and out case of the reticulated pigmentary type which Bloch and Sulzberger have described, but this diagnosis has to be considered

DR REUBEN FRIEDMAN Montgomery reviewed the subject of unilateral nevi in 1901 and found that this disease had been given some forty-eight different designations by that many different investigators, and each one had so qualified the appellation as to give some intimation of the causative factors involved according to the thought of that investigator He mentions the fact that linear nevi often follow the course of cutaneous nerves and sometimes are found along Voigt's lines I called the attention of some of our members tonight to the fact that the initial nevus on the arm follows the course of one of the superficial veins, and this also is mentioned by Montgomery as a possible causative factor—the lines following the distribution of cutaneous vessels Some other investigators, I think, ascribe the disease to some disturbance in growth of embryonic tissue, and others state that linear nevi run in the metameres or segments of the body

DR SIGMUND S GREENBAUM Some of those occur with ectodermal defects I could not see how in this case the lesions follow a nerve, unless it is the axillary nerve And one cannot ignore the fact that new spots are coming out on this child

DR FRITZ CALLOMAN (by invitation) This demonstration of a unilateral nevus—showing a straight linear course in its brachial part and a metameral distribution in its scapular part—appears significant Through decades the problem of the linear or metameral development of malformations and diseases of the

skin has been discussed and will continue to be studied. Linear development of moles usually is limited to the extremities. However, not infrequently this course has been observed also with moles of the body or face. Contrarily, diseases of the skin, such as neurodermatitis or scleroderma, when showing a linear development almost always have been observed on the skin of the upper or lower extremities, while their linear appearance on the body is extremely uncommon, and the diseases are not often found in the facial region.

The case directs attention to one of the old standard works of international dermatology which has not lost its significance up to the present time. I refer to A. Blaschko's memorable atlas published in 1902, under the auspices of the "Deutsche dermatologische Gesellschaft" (*Die Nervenverteilung in der Haut in ihrer Beziehung zu den Erkrankungen der Haut*, Vienna, W. Braumüller). In it the so-called "nevus-lines" have been systematically registered, tabulated and analyzed from material collected in an enormous number of reported cases.

As to the case under discussion, it is probable that an analogous observation may be found in Blaschko's atlas.

**Erythema Annulare Centrifugum** Presented by DR. CARROLL S. WRIGHT and DR. E. R. GROSS

R. B., a white man aged 60 years, presents, chiefly on the back, a number of asymmetric, annular, elevated, slightly reddened lesions, some of which are several inches in diameter. The lesions tonight have lost the annular appearance that they had when the patient was last seen, in December. For thirty years the patient has had an eruption, chiefly on the trunk and most pronounced on the back. This has been intermittently better and worse but has never disappeared. There are no local or constitutional symptoms.

DISCUSSION

DR. SIGMUND S. GREENBAUM: I saw this patient as a private patient about two years ago, and, just as tonight, he had a nodular eruption. The term "erythema annulare centrifugum" excludes a nodule. I told Dr. Wright that I did not think it was that, but there were lesions similar to erythema annulare centrifugum, and no doubt Dr. Wright saw the patient when he did have that type of lesion. But he does have nodules. I took a biopsy specimen and sent a section from one of the nodules to Dr. Weidman, and he made the provisional diagnosis—not clearcut—of mycosis fungoides, also mentioning aleukemic leukemia as a possibility. The blood picture, however, did not show anything of significance. He has no itching, and he has had the disease for thirty years, hence one would be inclined to exclude mycosis fungoides on that basis. I think that eventually, however, this will prove to be one of the lymphoblastomas. It reminds me of a case I saw many years ago of ichthyosiform erythroderma, which turned into mycosis fungoides.

DR. HERMAN BEERMAN: That patient had about three kinds of carcinoma in addition, but he is still living. His histologic picture, however, was clearcut two or three years ago.

DR. CARROLL S. WRIGHT: I have seen this man three or four times, and the picture does vary a great deal from time to time. On every other occasion he has had annular lesions slightly elevated and has never had this nodule before. I am still not willing to accept the diagnosis of mycosis fungoides, in spite of one nodule.

DR. MORRIS MARKOWITZ: How old is the lesion at the bottom of the chest posteriorly?

DR. CARROLL S. WRIGHT: That is the one I said I had never seen before. It has appeared in the last month.

DR. SIGMUND S. GREENBAUM: About two years ago I irradiated that nodule, and it disappeared. Now there has been a recurrence.

**Cutis Hyperelastica** Presented by DR MEYER L NIEDELMAN

R M L, a white girl aged 11 years, presents numerous scars as the result of injury on the left arm and forearm, both knees and legs. There is pronounced fragility of the skin, so that even slight trauma produces hematomas and wounds. The skin has a velvety texture, appears to have little fatty tissue and is smooth, soft and apparently somewhat thinned. It is elastic and on certain areas, especially the lower part of the arms, can be drawn out from the body for some distance. The patient also has hyperflexibility of the joints and small tumors under the skin. The anomaly became apparent at the age of 2 or 3 years, when the child began to walk. On slight trauma due to falling, the wounds remained open, refused to heal and necessitated suturing. Even then the wounds broke down and became infected.

The urine and the blood count were normal.

## DISCUSSION

DR MORRIS MARKOWITZ. This case can be taken as an example of the Ehlers-Danlos syndrome. The patient has the hyperelastic skin, and Dr Butterworth tested the tendons of the fingers and could flex them whichever way he wanted to.

DR THOMAS BUTTERWORTH, Reading, Pa. This is an interesting case because the process is asymmetric and because the tonicity of the skin in general is greatly diminished on the left side of the body. There is an increased hyperextension of the left thumb, but the right thumb can go back only a little more than normal. She had some trauma on the left side, which of course in the ordinary case could be coincidence, but with the hyperextension and the difference in tonicity it may mean something in the present case. It is the first case I have seen in which one side was involved more than the other.

DR SIGMUND S GREENBAUM. I showed a father and daughter about two years ago who had the entire tetrad which goes into the formation of this syndrome. These do not show them all. Only one of them has the tumors.

**Sycosis Coccigenica Suggesting Lupus Vulgaris, Toxicoderma** Presented by DR CARROLL S WRIGHT

C R, a white man aged 42, four years ago had a patchy eruption on the legs. The eruption soon appeared on the arms and then on the neck anteriorly and in the bearded region. While it has persisted, it has been intermittently better and worse. Seven roentgen ray treatments three years ago caused no improvement, nor did ultraviolet irradiation or local applications. He states that another dermatologist told him that it was tuberculosis of the skin.

## DISCUSSION

DR SIGMUND S GREENBAUM. I should like to offer the diagnosis of lupoid sycosis of Brocq—simple scarring with peripheral neuritis (?), not entirely a sycosis. Biopsy should show cicatrization at the center of the patch.

DR BERTRAM SHAFFER. I treated a patient with an eruption similar to this, who received injections of *Staphylococcus ambotens* plus the use of chloroxyquinolor (Squibb). He responded, but at the end of a year he had a relapse and came back. But at least he had a remission for a time.

DR ISADORE ZUGERMAN. I also saw that patient. I suggested a biopsy, but he would not consent to it.

DR JOHN F WILSON. I suggest that penicillin, both intramuscularly and locally, would be worth while in such a case. I have not seen any patients with the lupoid type of sycosis so treated, but I have seen one with sycosis vulgaris who did well.

DR SIGMUND S GREENBAUM. I have observed 2 cases of severe sycosis vulgaris in which large doses of penicillin were absolutely valueless. I would not recom-



mend it, it is a waste of time and money. I thought penicillin ideal when I tried it, but it did not have any effect. I used it by injection.

DR JOHN F WILSON Perhaps the combination would be effective.

DR SIGMUND S GREENBAUM Perhaps the penicillin was rubbed in with a wetting agent.

DR ISADORE ZUGERMAN This patient also has other lesions on his body and legs.

DR MORRIS MARKOWITZ On the lower extremities the eruption certainly looks like papulonecrotic tuberculid.

DR SIGMUND S GREENBAUM I did not pull out any of those involved hairs, but the patient said that when he did he observed a gelatinous material on the end of the hair, indicating a focal infection.

DR CARROLL S WRIGHT Frankly, I was puzzled by the case. I am inclined to accept Dr Greenbaum's diagnosis. I think that probably biopsy would be the answer, and I suggested that to the patient, but he refused to follow my suggestion.

DR REUBEN FRIEDMAN Is there a distinction between the diagnosis given by Dr Wright and lupoid syphilis?

DR SIGMUND S GREENBAUM Brocq gave the disease that name because of its cicatrizing nature.

DR CARROLL S WRIGHT It seems to me that this is just a recent development.

DR REUBEN FRIEDMAN I think that many of those lesions on his legs are neurotic excoriations. The patient told me that he just dug them out of the skin.

#### **Pityriasis Rubra Pilaris** Presented by DR CARROLL S WRIGHT

C F, a white boy aged 12 years, presents a widespread eruption of acuminate closely grouped papules. The extensor surfaces of the fingers showed decided involvement. The patient was presented in November 1944 for diagnosis (avitaminosis or early pityriasis rubra pilaris?). In spite of massive doses of vitamin A by injection and by mouth, the eruption has spread and become much more pronounced.

#### DISCUSSION

DR J M SCHILDKRAUT, Trenton, N J I suggest the use of vitamin B instead of vitamin A.

DR SIGMUND S GREENBAUM I shall have to agree with Dr Wright's first diagnosis. I do not think the eruption is pityriasis rubra pilaris. The papules are a little larger, they are not entirely follicular, and they are not acuminate, as in pityriasis rubra pilaris. The fact that they did not clear with vitamin A is, I think, against that diagnosis. Since vitamin A has been introduced in the treatment of Darier's disease, it has been used in cases of pityriasis rubra pilaris, often with benefit. I have 1 case in which it cleared completely. In this case the eruption does not have the rasplike feeling, and the papules are a little larger and not acuminate, and if one looks where the hairs ought to be on the dorsa of the proximal phalanges there is just one finger which has an involvement of the pilosebaceous follicles. I saw this child before Dr Wright did, and we both thought that the eruption was lichen scrofulosus, and I still think it is. I made a patch test with tuberculin, and the reaction was positive. Why not have a dark adaptation test? I know that the physicians of Mayo Clinic do not believe much in the dark adaptation test for vitamin A deficiency, but it is worth while seeing what develops from it.

DR CARMEN C THOMAS One could also determine the amount of vitamin A in the serum.

#### **Hairy Tongue** Presented by DR CARMEN C THOMAS

M B, a white man aged 36, presents on the posterior third of the tongue a heavy, yellow-brown deposit composed of elongated papillae, which give the tongue

a furry appearance. The papillary projections are easily curetted off without pain or bleeding and are seen to be composed of fine, threadlike material. The disease had its onset about three years ago, when the patient noted a furry appearance of the posterior portion of his tongue. It became accentuated and much more pronounced in the past six months, when a dark discoloration appeared. There are no subjective symptoms other than a bad taste, which makes him disinclined to eat.

Culture of the papillary curetted material yielded *Monilia*.

The serologic reaction of the blood for syphilis, by the Kolmer, Kline and Eagle procedures, was negative.

The patient has been given a mouth wash of sodium perborate and one of hydrogen peroxide.

#### DISCUSSION

DR MORRIS MARKOWITZ. That pigmentation has a great deal to do with vitamin administration. Nicotinic acid is likely to produce black tongue.

DR SIGMUND S. GREENBAUM. But this is not merely black tongue, it is hairy tongue.

DR CARMEN C. THOMAS. These hairs come off without any difficulty and can be curetted off and are extremely long.

DR HERMAN BEERMAN. I treated a patient with vitamin B, and she got well comparatively soon.

DR MEYER L. NIEDERMAN. I treated a patient by spraying the tongue with ethyl chloride and curetting thoroughly and then cauterizing with saturated solution of trichloroacetic acid.

DR THOMAS BUTTERWORTH, Reading, Pa. Wise, I think, recommends 50 per cent trichloroacetic acid. I used that in a case with success.

DR HERMAN BEERMAN. I think one of the reasons for my use of vitamin B was that one sees peculiar tongues in pellagra and other diseases due to vitamin deficiencies, and that is the only sensible reason for trying it.

DR SIGMUND S. GREENBAUM. Black tongue in dogs was cured by Goldberger with vitamin G, later called riboflavin, but there is no relation between black tongue in dogs and the disease presented by this patient.

### NEW YORK DERMATOLOGICAL SOCIETY

Hans J. Schwartz, M.D., *President*

George C. Andrews, M.D., *Secretary*

Jan 23, 1945

#### Tinea Capitis in an Adult. Presented by DR. GEORGE C. ANDREWS

This patient has been treated for an infection of the scalp since February 1944. The eruption, which had been present for two months prior to that time, is on the vertex and consists of erythema with small atrophic spots, follicular pustules, depressed scars and spotty alopecia. In addition, there is a persistent redness and scaling, with occasional vesicles and pustules on the right palm. There has been a similar eruption at the base of the right ring finger, and the nails of the second and third fingers on the right hand are thickened, discolored and friable. Cultures from the skin on the palms and from the finger nails showed *Trichophyton gypsum*, and cultures of material from the scalp have repeatedly shown *T. gypsum*. Several broth cultures from the scalp have been regularly sterile.

#### DISCUSSION

DR HOWARD FOX. Twenty years ago Dr. R. W. Fowlkes and I reported 3 cases of tinea capitis in adults, all in Negroes (*ARCH. DERMAT. & SYPH.* 11:446,

[April] 1925) The following year, I reported a fourth case, the patient being a mulatto. In 1 case the disease was due to a *Trichophyton* and in 3 to *Microsporon*. After a diligent search in the available world literature, we were able to find reports of about 70 cases, exclusive of those in Japan, where the disease in adults is less of a rarity. Of the 70 cases cited, the diagnosis had been made by microscopic examination or culture in 53 cases.

DR GEORGE M. LEWIS It is interesting that with the epidemic among children very few cases have been encountered among adults. In any case, I think that it is always well to examine the parents, or at least the mother, when she comes in with the child.

### **Vesiculobullous Eruption Involving Vitiliginous Areas of the Perivulval and Perianal Regions** Presented by DR MAURICE J. COSTELLO

I. G., an Italian-born woman (a private patient) aged 75, has had a pruritic vesiculobullous eruption on the vitiliginous areas of the perivulval and perianal region for three years. Severe excoriations are seen from time to time. On several occasions large flat bullae have been observed.

There are a narrowing of the introitus and atresia of the anal and vaginal orifices, in addition to atrophy of the internal genitalia. There is no history of ingestion of drugs. Biopsy has been performed, but the report is not yet available.

#### DISCUSSION

DR GERALD MACHACEK I offered the diagnosis of lichen sclerosus et atrophicus. I have seen similar diseases occurring on both male and female external genitalia, and I have also seen cases with bullae. Recently in the dermatologic literature a controversy has been going on regarding the appearance of bullae in lichen sclerosus and scleroderma.

DR A. BENSON CANNON When I first examined the lesions between the folds of the buttocks I expressed the opinion that the case was one of lichen planus atrophicus with bullous lesions. On further inspection, I found some lesions typical of that disease on the left side of the trunk. I recently saw a case similar to this one but with more extensive lesions, presented by Dr. Weiss at the dermatologic clinic of the Southern Medical Association in St. Louis. It is most interesting that the lichen sclerosus et atrophicus is confined to the vitiliginous areas between the folds of the patient's buttocks.

### **Subacute Lupus Erythematosus Disseminatus** Presented by DR HOWARD FOX

Mrs. L. M. L., aged 30, a bookkeeper, recently married, had never had any previous illness. Her tonsils were removed in early childhood, the menses were irregular up to the age of 21, and her circulation has always been poor. One brother had had a mild attack of pulmonary tuberculosis. The patient had plastic operations on the nose and ears for cosmetic reasons. Roentgenologic examination of the teeth showed them to be in good condition.

For about five weeks, beginning Nov. 1, 1944, she had ephemeral attacks of redness, itching and puffiness of the eyelids and areas just above the eyebrows. These attacks lasted three or four days. The present eruption began on Dec. 15, 1944, above the eyebrows, and within a month it had spread to involve the cheeks, chin, parts of the ears (right lobule and left concha), abdomen and heels.

The lesions on the face are fairly well defined large coin-sized patches. They are superficial, red, dry and nonitchy and show some scaling. The present eruption followed an exposure to ultraviolet radiation, when she was standing beneath an ultraviolet lamp, while giving her husband a massage. She stated that she had always been sensitive to sunlight.

There is an oval patch on the left upper quadrant of the abdomen, measuring  $4\frac{1}{2}$  by  $2\frac{1}{2}$  inches (11 by 6 cm.), which is yellowish red and on which are a few

millet seed-sized flat red papules. The heels are dull red and present the same type of papules which are present on the abdomen. The red color of the papules disappears completely under diascopic pressure, leaving no suggestion of apple-jelly nodules.

The patient is 5 feet (152 cm) tall and weighs 100 pounds (45.4 Kg). There is a decided livedo reticularis of the lower extremities from the knees to the ankles. An examination of the blood at an army hospital showed hemoglobin 81 per cent, erythrocytes 4,210,000 and leukocytes 5,800, with a differential ratio of 65 per cent polymorphonuclear leukocytes and 34 per cent lymphocytes. The urine was normal. Recently, the basal metabolic rate was + 12 per cent, whereas eight years ago it was - 40 per cent. Since then she has taken thyroid continually.

#### DISCUSSION

DR A BENSON CANNON. I should consider this case one of discoid lupus erythematosus with disseminated lesions. She appears unusually well. The lesions above each eyebrow are oval and have clear atrophic centers that are lighter in color, with red scaly borders and some dilated follicles. The areas on the left side of the body and legs are superficial eczematized patches that I could not interpret as lupus erythematosus. If further study by Dr Fox should prove the case to be one of subacute lupus erythematosus, I should advocate treatment with strong solution of iodine U S P, injections of crude liver extract and a high caloric diet. I have recently seen 2 patients with this disease who were treated successfully by other physicians.

DR MAURICE J COSTELLO. If Dr Fox has not already had the sedimentation tests performed, I think it would be advisable to have them done. I agree with Dr Fox's diagnosis.

DR GEORGE M LEWIS. The patient has a fever and a low leukocyte count. While she looks surprisingly well, I am in favor of the diagnosis as presented.

DR EUGENE F TRAUB. I think that one of the confusing features about the word "discoid" is that there seem to be two types of these lesions: the type so commonly seen in the past, which caused a great deal of damage to the patient's face, and the type of lupus erythematosus which has changed considerably over a period of years. Now the destructive type is seen rarely. The type to which Dr Cannon refers is superficial, in which destruction is not great and there is healing with no scarring. I believe that the case presented here tonight is one of the superficial discoid type, in which the acute process, if not present now, is certainly subacute and fatal termination will ensue.

I presented a young woman before the society whose eruption apparently cleared, after hospitalization at the New York Post-Graduate Medical School and Hospital, where she had been treated with iodine and transfusions. She returned, and despite another transfusion and iodine she rapidly grew worse and died. I am not at all sure whether these remissions do not take place more or less spontaneously, at least they are not lasting, and the prognosis has to be determined over a period of years.

DR HOWARD FOX. I agree with the last two speakers that this patient has a serious disease. On numerous occasions the lesions have appeared and remained only two or three days, indicative of the disseminate, rather than the fixed, type of the disease. I had intended to try Dr Cannon's method of using strong solution of iodine U S P and should like to ask Dr Cannon whether his method would be harmful for the fixed type of this disease.

DR A BENSON CANNON. I suggest that Dr Fox give his patient strong solution of iodine for six months or longer. It is not always easy to differentiate between the various types of lupus erythematosus, especially when the lesions are generalized.

DR GEORGE C ANDREWS. In many cases of acute disseminated lupus erythematosus one gets little or no eruption but, rather, involvement of the glands and

viscera This woman has fever and a low leukocyte count, and I think that she has a serious form of the disease I agree with Dr Traub that these are remissions and that they do not mean much The disease sometimes goes on for years before it terminates fatally One cannot be too complacent over the results of a few months' treatment

### Two Cases for Diagnosis (Unguis Incarnatus?) in a Brother and Sister Presented by DR HOWARD FOX

M W S, aged 21, an electrical engineer, has suffered from an eruption of his toes for the past seven years The great, second and third toes of each foot show masses of exuberant granulations in the lateral nail folds and beneath the free borders of some of the nails The appearance of ingrowing toe nails is suggested There are moderate pain and tenderness but not enough to prevent a considerable amount of walking There is decided hyperhidrosis of the feet The disease was a cause for rejection by the army

Microscopic and cultural examinations for fungus have given negative results Staphylococcus aureus was recently obtained on culture

The lesions have been treated by other physicians with roentgen rays, antiseptic ointments and lotions and by surgical excision On two occasions the lesions were excised by a surgeon, a general anesthetic being used Eventually, the disease recurred

L S, aged 11, a sister of M W S, has had a similar lesion for about two months on the right great toe There are no other lesions on the feet suggestive of a fungous infection A microscopic examination revealed fungi The exuberant granulations have been curetted and cauterized half a dozen times, with no permanent results

#### DISCUSSION

DR A BENSON CANNON It is difficult to say how the lesions of granuloma pyogenicum originated Judging from the appearance of some of the nails and from the history, one might suspect a fungous infection Mild mercurial ointment applied thickly to each lesion and kept on constantly for two weeks might prove beneficial, if not curative Should the cultures demonstrate pyogenic organisms, one might use wet dressings of penicillin or the ointment

DR EUGENE F TRAUB I think that these are two of the most unusual deformities of the feet I think that they resulted from some type of low grade pyogenic infection, producing this granulation tissue, certainly in the young girl it looks almost like a pyogenic granuloma The only suggestion for treatment I can think of is to remove the entire nail and graft skin over the entire area, the entire nail should be ablated permanently

DR JOHN C GRAHAM Both patients have highly convex nails, pressing down into the tissues, and any treatment short of removal of these nails would be of no great value I think that Dr Traub's suggestion of complete removal is the only possible cure for nails pressing into the tissues as these are

DR GEORGE M LEWIS If a fungous infection is considered, the clinical picture can be explained on the basis of acute Trichophyton gypsum infection involving the paronychia tissues Some of the nail plates are definitely diseased I think it unusual to see brother and sister with a pyogenic infection I favor a diagnosis of fungous infection

DR MAURICE J COSTELLO The surgeon apparently thought that this was an ingrown toe nail I do not think that this condition is unusual, because it has occurred in several members of the same family, and I believe that there is superimposed infection Wedges have already been taken out of the sides of the nails

DR HOWARD FOX Puzzling features in this case are that a brother and sister are affected and that the brother has a symmetric involvement of three nails on each foot In view of the failure of treatment during the past seven years, I have advised that the affected toe nails be permanently destroyed

**Pyoderma Faciale—Unimproved by Local and Parenteral Penicillin Therapy** Presented by DR. MAURICE J. COSTELLO

H C, a graduate nurse aged 22 (a private patient), was first seen by me, on Nov 21, 1944. She stated that she had had a pustular eruption on her face for six months. It consisted of numerous large painful cystic pustules, which discharged light greenish purulent material when incised. Interspersed with the larger lesions there were a number of tiny superficial thin-walled pustules. The lesions were discrete and coalescing. No comedos were present, and although the skin was red the picture was not that of rosacea. The patient did not suffer from indigestion or constipation. Her treatment has consisted of weekly treatments of low voltage roentgen rays, penicillin ointments, 500 units per gram of base, and 2,000,000 units of penicillin by intramuscular injections. Tyrothricin compresses were used. Ten drops of hydrochloric acid, diluted in a glass of water at meals, was administered.

DISCUSSION

DR. A. BENSON CANNON: I understand that this disease responds to treatment with penicillin, and I advocate a continuation of that medication. I think that the increase of redness in and around the lesions might be interpreted as a reaction to the penicillin that was given this morning. I have noted similar reactions in cases of pyogenic infections, reactions that lasted for the first three or four days of treatment with penicillin and on the fourth or fifth day subsided, the patients showing great improvement. Often there was a complete cure in seven to ten days. Should penicillin fail to cure the patient, I should then advocate that the cystic lesions be irrigated with a 5 per cent phenol solution every four or five days until they have healed.

DR. HOWARD FOX: The term "pyoderma faciale" is a convenient one for cases that are not definitely ones of acne vulgaris or of rosacea. This patient is rather young to suffer from rosacea, and she gives no history of a gastrointestinal disorder. On the other hand, she presents no comedos, which are the primary and essential lesions of acne.

DR. GEORGE C. ANDREWS: The question is whether this woman has cystic acne, pyoderma faciale or rosacea. One might argue at length on these points. I believe that her sinuses ought to be examined. I have recently had a nurse under my care whose face looked much worse than this. She was not helped by penicillin or sulfonamide drugs. She had pansinusitis, and an operation has cured her. A roentgenogram of this patient's teeth should be made for focal infection.

DR. EUGENE F. TRAUB: I agree with Dr. Andrews that focal infection might play a considerable role in the case of this woman. Another point that might have a bearing on the lack of result from penicillin therapy is that this patient is at present receiving roentgen ray therapy, and small doses have been given right along. This type of eruption, in my experience, has always become worse with roentgen ray therapy, no matter how small the dose. I do not know whether this has been the universal experience of the other men. I would discontinue roentgen ray therapy, and perhaps the penicillin might then show results. Another suggestion is that this type of patient might do well with isotonic solution of sodium chloride, administered intravenously, starting with injections of 50 cc and bringing this up to 100 to 200 cc on subsequent doses. This is a simple and harmless procedure.

DR. RAY H. RULISON: This patient says that she has no lesions on her back, but I noticed several pustules there. I think the fact that she has some pustulation on the back and no special redness on the nose eliminates the diagnosis of rosacea. As for the fact that the patient got worse with roentgen ray therapy, as Dr. Traub pointed out, that has been my experience. Patients get worse temporarily because of the effect of roentgen rays on the leukocytes. I think that if roentgen ray therapy is continued improvement will follow.

DR. ANTHONY CIPOLLARO: I think that this is a case of severe cystic acne vulgaris. The large fluctuant cysts should be evacuated. There is no evidence to

substantiate the statement that roentgen ray therapy makes this disease worse. In fact, it has been my experience that all patients with cystic acne vulgaris improve or get completely well when treated with roentgen rays. I generally treat this disease with filtered roentgen rays, using a 3 mm aluminum filter and administering a dose of 75 to 100 r per week.

**DR MAURICE J COSTELLO** I presented a similar patient eight months ago at the Manhattan Dermatologic Society. She received penicillin with improvement, and later this was followed with roentgen rays. She was completely cured, in spite of the fact that the eruption had been persistent and resistant to treatment for eight months. The patient under discussion received fractional doses of roentgen rays but has not received any in the past three weeks. Exacerbation of acne is the rule rather than the exception when the first six to eight treatments with roentgen rays are administered.

#### **Tinea Capitis, Without Alopecia** Presented by **DR GEORGE C ANDREWS**

**B K**, a 6 year old girl, had a rash on the scalp last August. About the same time her mother had a spot of ringworm on her knee and one at the back of her neck. The family had two Persian cats, which may possibly have been the source of the infection. The mother's lesion was cured by a local physician. He did not treat the child's scalp because he did not think that the rash was ringworm.

The clinical appearance of the child's scalp shows no alopecia or broken-off hairs. There are no pustules, but there is a mild crust formation resembling dandruff on the right side of the vertex and in the front of the scalp. Examination with a Wood filter shows pale green fluorescent bodies on the hair. Microscopic examination of the hairs shows spores and mycelium within the shaft of the hair. Cultures have grown *Microsporon lanosum*.

With local treatment with a lotion of thymol, salicylic acid and iodine in alcohol there has been much improvement, and today under the Wood filter the hair shows no fluorescence and the scalp appears cured.

#### DISCUSSION

**DR EUGENE F TRAUB** This happens occasionally. I had a youngster in the clinic with what looked like ordinary dandruff, I sent him up for examination under a Wood filter, and I got a culture positive for fungi.

**DR GEORGE M LEWIS** This is unusual from the fact that the organism is a microsporon, and in that case one would expect a loss of hair.

#### **A Case for Diagnosis (Parapsoriasis?)** Presented by **DR HOWARD FOX**

**Mrs B R F**, aged 36, has suffered from a generalized, symmetric profuse eruption for the past seventeen years. During this time there has been no appreciable change in the lesions, except that they are more noticeable in the winter than in the warm months.

The eruption involves mainly the sides of the trunk, the posterointernal aspect of the upper and lower extremities and the buttocks. It consists of diffuse areas which are red, superficial and dry, with some fine scale and with well defined borders in places. The scalp shows moderate dandruff. The face, hands and feet are free of any eruption. There had never been any itching until the past two months, when she was worried about a serious illness of her mother. No scratch marks are present. She has never received any benefit from treatment, including long exposures to sunlight during the summer.

Biopsy was performed by a dermatologist eight years ago, and a provisional diagnosis of "neurodermatitis" is said to have been made. Four years ago a second biopsy, by another dermatologist, showed a "chronic eczema." No clinical diagnosis, however, was made at this time.

Recently, roentgen rays have been given to several areas on one side of the body as a therapeutic test. Five areas have been treated at weekly intervals with 75 r of unfiltered radiation with no improvement.

The patient has suffered from occasional attacks of spastic colitis but otherwise appears to be in good general health. She is 5 feet (152 cm) tall, and weighs 137 pounds (62 Kg).

## DISCUSSION

DR GERALD MACHACEK I favor the diagnosis of parapsoriasis.

DR HOWARD FOX My reasons for excluding mycosis fungoides are the duration of seventeen years without any appreciable change, the absence of itching, the absence of any suggestion of mycosis fungoides in two biopsies and the lack of response to five roentgen ray treatments (75 r each), given once a week for five weeks. The most likely diagnosis, in my opinion, is parapsoriasis en plaques.

### A Case for Diagnosis (Dermatitis Factitia, Tuberculid?) Presented by DR GEORGE M LEWIS

H D, a registered nurse aged 29, was first seen on November 17, when she stated that for six years she had had recurrent lesions around her ankles. Three years ago she stopped nursing and returned to her home in Maine, and during the year spent at home she had no lesions. Six months after she returned to work they again began to develop, and they have been more numerous for the past few months.

At present there are four purpuric lesions which are flat or slightly elevated and discrete, located on the outer side of the left ankle. One similar lesion is present on the right ankle. The lesions exhibit what appear to be necrotic centers. There are a number of slightly depressed scars on various sites over the ankles.

Through the courtesy of Dr A. Benson Cannon, details of examinations made in 1941 are available. Biopsy ruled out Majocchi's disease and Kaposi's disease. According to Dr Machacek, the section from the lesion showed a vasculitis. Bacteriologic studies revealed *Staphylococcus aureus*, the Wassermann reaction of the blood was negative, the blood count was normal. Roentgenologic studies of the thighs and legs revealed nothing abnormal in the soft tissues or bones. The urine was normal. A cutaneous test with tuberculin in a 1:100,000 dilution elicited a negative reaction. There was no clinical effect from the ligation and injection of the left internal saphenous vein.

## DISCUSSION

DR EUGENE F. TRAUB What the name of this disease is I do not know, but I have seen it on several occasions. I do not think it is dermatitis factitia, it is some type of change in the vessels that produces first what looks like purpuric lesions and then a central necrosis, occurring on the lower extremities.

DR GERALD MACHACEK Three years ago I saw microscopic preparations of lesions removed from this patient, and I offer only the diagnosis of vasculitis. I cannot classify the disease more precisely.

DR MAURICE J. COSTELLO I agree with Dr. Traub, but I think that the toxin is tuberculous. A patient with this eruption had clearing with injections of gold sodium thiosulfate.

DR A. BENSON CANNON I think that this eruption is an artefact.

DR GEORGE M. LEWIS I am obliged to Dr. Cannon for giving me a resume of the findings while the patient was hospitalized at Presbyterian Hospital. The biopsy rules out tuberculosis and other granulomatous diseases, but Dr. Machacek reported evidence of vasculitis. Results of all routine tests were either normal or negative, including a bacteriologic culture and a roentgenogram of the chest. It struck me as unusual that this patient stopped work and went away for a year simply because of these lesions, yet she does not say that they bothered her too much. That to my mind is in favor of dermatitis factitia, but I am at a loss to understand how one can produce lesions of this type. If it is an artefact, it is unusual.



**Mycosis Fungoides** Presented by DR GEORGE C ANDREWS

A R, a man aged 48, presents an eruption that began in 1933 and has been present intermittently ever since, being severer recently. It is widespread, consisting of variously shaped configurate flat or slightly elevated, sharply defined, erythematous, slightly scaly lesions. Some of these are infiltrated plaques and show variegated tints of pink and red mixed with yellow. The eruption is bizarre in appearance, many of the lesions being polycyclic. There are a few pea-sized tumors. Where some lesions have disappeared, there is depigmentation. There is no lymphadenopathy, and the liver and spleen are not palpably enlarged. The biopsy specimen from one of the spots on the trunk was irregularly acanthotic. In the middle and in the upper part of the cutis there was a cellular infiltration mostly perivascular and polymorphous, with fairly large histiocytes (epithelioid) in evidence. A reticulum was faintly suggested. There was an occasional mitotic figure in the large cells. These features are sufficient to warrant the diagnosis. The microscopic diagnosis is "mycosis fungoides." The Wassermann reaction of the blood was negative. The patient has been receiving roentgen ray treatments. The blood count showed hemoglobin, 89 per cent, white blood cells, 8,750, red blood cells, 4,700,000, color index, 0.95, polymorphonuclear neutrophils, 73 per cent (mature, 60 per cent, immature, 13 per cent), lymphocytes, 22 per cent, basophils, 1 per cent, eosinophils, 4 per cent, and no mononuclears. The red blood cells appeared normal.

## DISCUSSION

There was no discussion of this case.

**Lunula Cyanea** Presented by DR GEORGE C ANDREWS

Since the birth of her last child, in 1941, Mrs B M, aged 39, has had a bluish discoloration that looks like cyanosis of the lunulae of the finger nails. This bluish discoloration is permanent, unchanged and unexplainable. There is no discoloration of the lunulae of the toe nails, but she has no moons on the toe nails, and the nails themselves appear perfectly normal. She has had two thorough cardiovascular examinations which revealed completely normal conditions. There is no abnormal pigmentation on the body or in the mouth, nor is there a history of her having taken medicines which might cause such a discoloration. There has not been any blanching of the hands or acroasphyxia, and plunging the hands into cold water causes no change in the coloration.

## DISCUSSION

DR HOWARD FOX. The patient had a mild type of clubbed fingers, which would suggest pulmonary or cardiac changes.

DR JOSEPH C HATHAWAY (by invitation). I noticed a swelling about the proximal half of the nails of all the fingers in addition to the discoloration. I do not know whether this means anything.

DR MAURICE J COSTELLO. When I questioned her, she stated that the otolaryngologist had been using neo-silvol packs in her nose. I cannot understand why she does not have discoloration about the nose if she has argyria. I believe this can be ruled out by chemical examination.

DR EUGENE F TRAUB. I think that the amount of silver this woman has been taking makes it questionable whether this discoloration is argyric or not. I think that it is more likely to be a condition associated with some pulmonary process.

DR GEORGE C ANDREWS. The lungs have been examined by roentgenographic and fluoroscopic procedures within the last three months. She has had two thorough examinations by internists in the city. There is nothing wrong with her lungs or cardiovascular system.

**Lupus Erythematosus of Unusual Type (Morphea-like Epithelioma?)**

Presented by DR MAURICE J COSTELLO

B V, a man aged 32, a private patient, was first seen by me, in June 1940. At that time he had a lesion which had been present for about seven months on the right temporofrontal region near the hair line. It covered a rectangular-shaped area of scarring, enclosing a spindle-shaped reddened, infiltrated, slightly raised area of waxy appearance with several sharply circumscribed ulcerations, from the size of a pinhead to that of a pea. This lesion was destroyed under procaine hydrochloride anesthesia. In February 1941 at the upper posterior angle of the old wound there appeared an irregular dime-sized reddened fissured crusted infiltrated lesion with a pearly border. Roentgen rays (1,000 r) were administered to this lesion and brought about its complete involution. Since that time there has been a gradual extension of a slightly raised skin-colored border which enclosed an area of atrophy and central crusting and telangiectasia. A biopsy specimen was taken from the active border, and the histologic diagnosis was reported by Dr Wilbert Sachs as lupus erythematosus. The microscopic description follows:

"There is a moderate cellular infiltration in the upper part of the cutis and about the adnexa. In the subepidermic region is tremendous basophilic degeneration. The overlying epidermis is moderately acanthotic and the follicles dilated and filled with horny plugs. The cellular infiltration is composed of small round and wandering connective tissue cells. The elastic tissue is clumped beneath the epidermis, there is no evidence of epithelioma or morphea."

The patient is presented for diagnosis and suggestions as to therapy.

## DISCUSSION

DR RAY H RULISON: I think that this man has a malignant tumor and not lupus erythematosus.

DR EUGENE F TRAUB: I agree with Dr Rulison. I think that this is a morphea-like, basal cell epithelioma, notwithstanding the histologic examination.

DR GEORGE C ANDREWS: I agree that this is a basal cell epithelioma.

DR MAURICE J COSTELLO: I have treated this lesion as a basal cell epithelioma with destructive measures on several occasions, but Dr Sachs states in his histologic report that the patient has lupus erythematosus.

**Bites from Sheep Ked (*Melophagus Ovinus*)** Presented by DR GEORGE M LEWIS

K M, a man aged 32, a wool packer, has had an eruption for ten months which began on the inner aspects of the thighs and gradually spread to the ankles. Occasionally it would spontaneously disappear. When first observed, in November, there was an eczematous eruption on the areas noted, consisting of erythematous exudative plaques. There were also discrete lesions consisting of macules with a central punctum. Some solitary lesions were also noted, affecting the penis, fingers and extremities.

With treatment the eczematous eruption responded satisfactorily. However, the pruritus has remained, and new solitary purpuric lesions have continued to form. Because individual lesions had the appearance of insect bites, the patient was hospitalized and routine studies were undertaken, without any positive results. Some of the live sheep keds were applied directly to the skin and were observed to bite the patient. This experimental area on the back still exhibits the remains of the lesions.

## DISCUSSION

DR GERALD MACHACEK: Several months ago I saw a wool sorter with a similar eruption. The lesions were pustular and had such a distribution that the disease simulated severe scabies. Lesions on the flank, however, suggested insect bites clinically. Remembering that there were such arthropods as sheep lice or

ticks, I so diagnosed the case and have in my laboratory a collection of these arthropods

DR GEORGE M LEWIS This case is of interest because I cannot find its counterpart in the literature, although word from the West, where the wool comes from, is that these parasites are commonly seen. I have looked through the available literature and have found no information of any value. Books on parasitology did not state that the ked is parasitic to man. In sheep it does carry disease which causes wasting but which apparently is not transferable to human beings

#### **Epidermolysis Bullosa** Presented by DR GEORGE C ANDREWS

V B, a woman aged 29, has had an eruption since the age of 3 years, with blisters on the palms and soles which have continued to appear without intermission since that time. The patient's brother has a similar eruption but to a worse degree, and his knees are also affected. The patient's mother and father are first cousins. She was referred by Dr Nathan Beers for an opinion.

The palms and soles show a general erythema and exfoliation studded by numerous small vesicles. There are also epidermic cysts on the rims of the ears and a suggestion of atrophy at the tips of the fingers. She has bilateral nystagmus

#### DISCUSSION

DR HOWARD FOX I would never have made the proper diagnosis without the history. The eruption suggested a dermatitis repens or pustular psoriasis. No bullae were present. As, however, the disease has been present since the age of 3 years and is familial, I must agree with the diagnosis of Dr Andrews.

DR A BENSON CANNON I do not recall having seen a case of epidermolysis bullosa similar to this one, and I could not make that diagnosis for this patient. There is a hyperkeratosis of the palms and soles with peeling, and there are no vesicles and no scarring.

DR EUGENE F TRAUB I should like to suggest that a more detailed history be obtained from the patient. She states that she removes skin from the area of the nails and that there is a definite tendency to thicken. If the blisters have actually been seen and another member of the family has a similar eruption, then the diagnosis might be accepted. But I would look on it as keratosis palmaris and plantaris which the patient has altered by treatment with salicylic acid and other medicaments and particularly by pulling off the skin herself.

DR GEORGE C ANDREWS This patient has not had salicylic acid for at least four months. As far as picking the skin is concerned, this is commonly seen wherever such exfoliation occurs, with little particles to be picked off. I have not seen any horny thickening that looked like keratosis palmaris et plantaris. The brother has had it on the knees as well as on the extremities. I asked the patient to bring her brother, but she said that because of the eruption he was confined to bed a good part of the time. I will go into the history more fully. I realize that this is not a typical case of epidermolysis bullosa, but I believe that it is an abnormal type of this disease.

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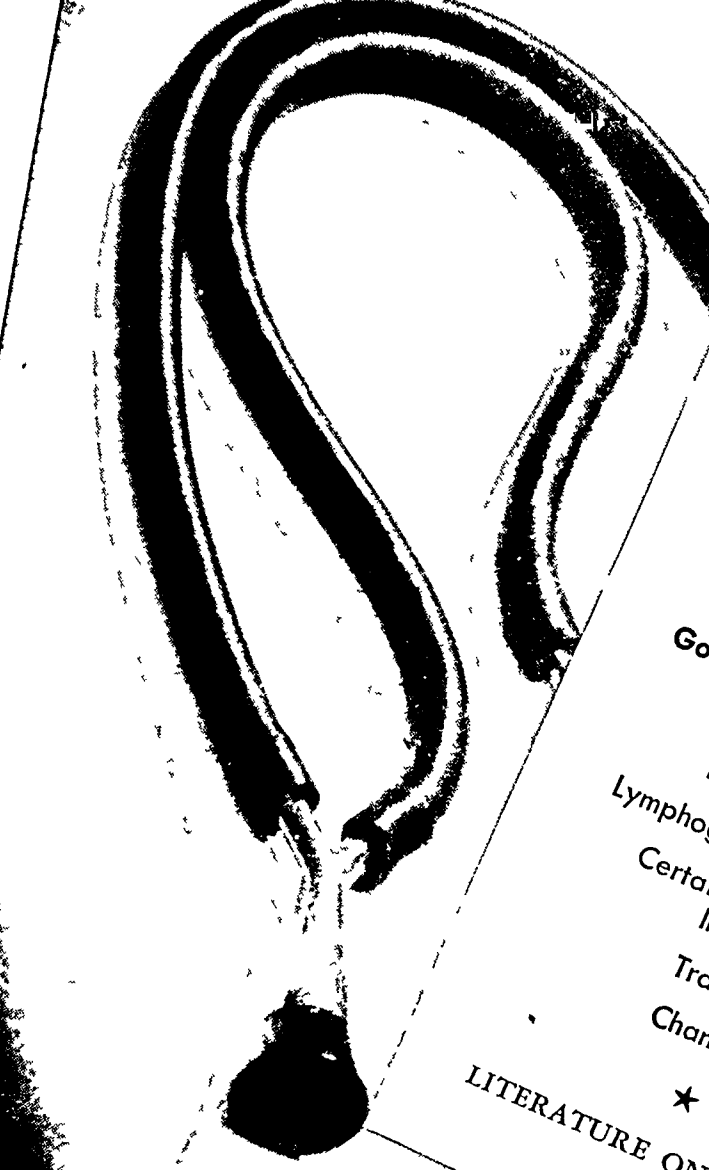
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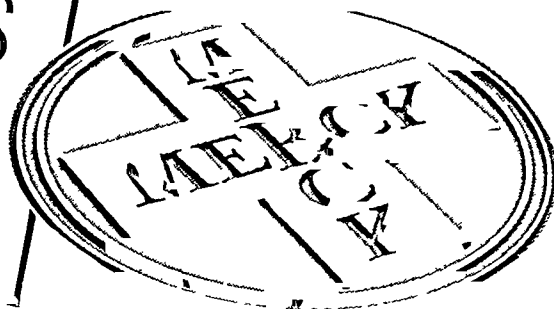
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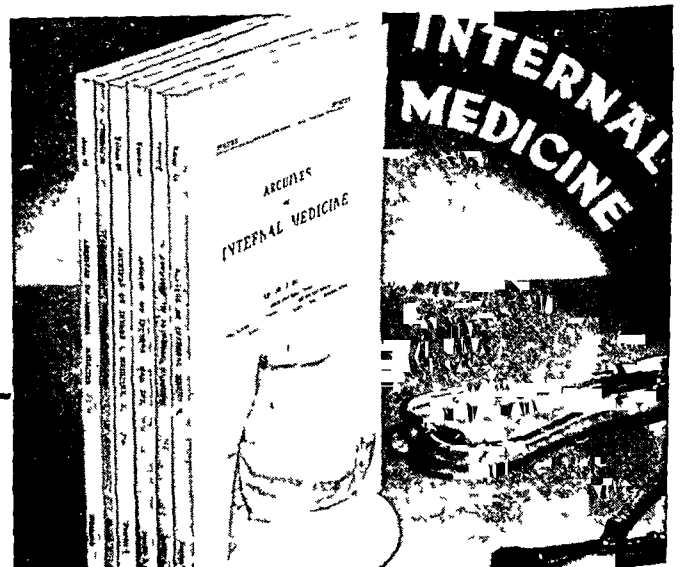
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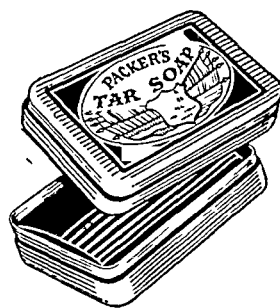


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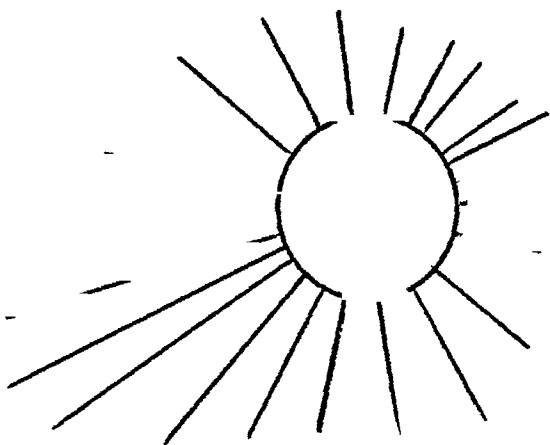
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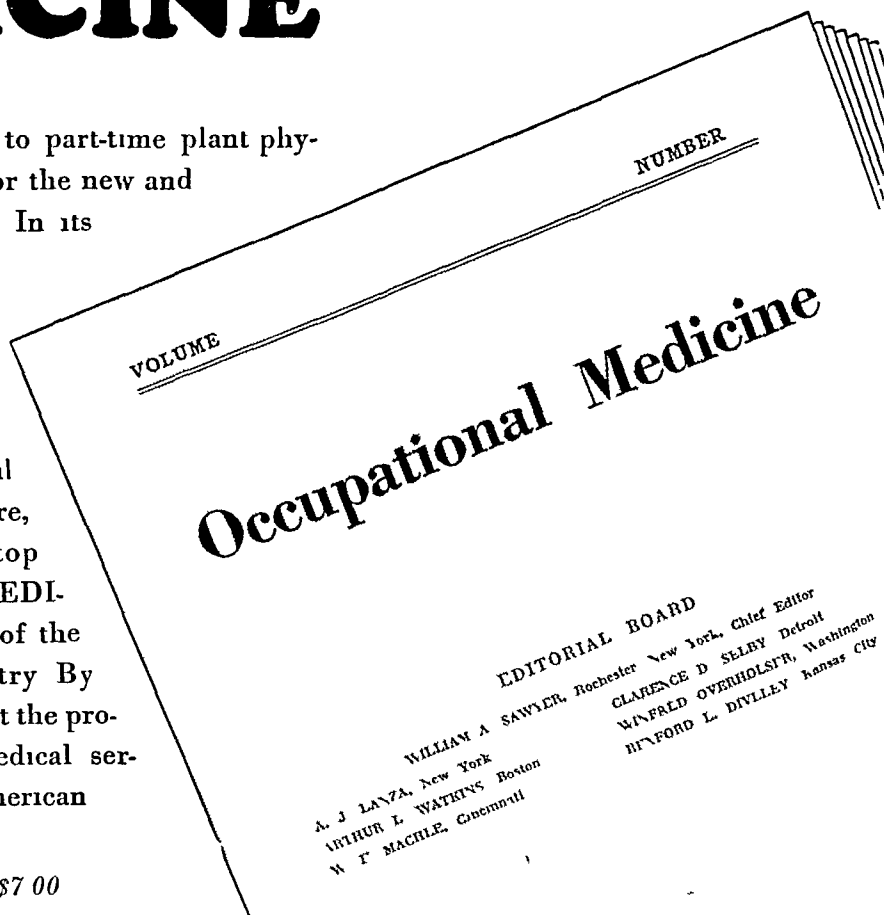
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#### Monday, November 4

A M	<i>Fundamentals of Allergy</i>
8 00 9 00	Registration
9 00 9 10	Address of Welcome WILLIAM HARVEY PERKINS M D, Dean, Jefferson Medical College Philadelphia Pennsylvania
9 10 10 00	Role of Histamine in Allergy HAROLD A. ABRAMSON M D Columbia University, New York, New York
10 00 11 30	Physiological Aspects of Allergy CHARLES T. CODE M D Mayo Clinic Rochester Minnesota
11 30 12 30	Pathology of Allergy MORTON McCUTCHEEN, M D University of Pennsylvania School of Medicine Philadel- phia, Pennsylvania
12 30 12 45	Orientation GEORGE E. ROCKWELL, M D Chairman
P M	<i>Fundamentals of Allergy and Therapy</i>
2 00 3 00	Immuno-Chemical Aspects of Allergy FRED W. WITTICH, M D Minneapolis Minnesota
3 00 4 00	Anti Histamine acting Substances RALPH L. MAYER M D Chief Bacteriolo- gist Ciba Pharmaceutical Products
4 00 6 00	Clinical Use of Histamine BAYARD T. HORTON M D Mayo Clinic, Rochester Minnesota
7 30	Informal Dinner Speaker LEON UNGER M D President American College of Allergists Subject <i>Opportunities and Pitfalls in Allergy</i>

#### Tuesday, November 5

A M	<i>Therapy</i>
9 00 9 45	Value of X Ray in Allergy, Diagnosis and Treatment PAUL C. SWENSON M D, Professor of Ra- diology Jefferson Medical College Phila- delphia Pennsylvania
9 45 10 30	Medical Emergencies in Allergy J. WARRICK THOMAS M D Graham Thomas Clinic Richmond Va
10 30 11 00	Antibiotics in Allergy HOBART REIMANN, M D Professor of Medicine Jefferson Medical College Phila- delphia Pennsylvania
11 00 11 30	Vaccines Their Preparation and Use GEORGE E. ROCKWELL M D Milford Ohio
11 30 1 00	Materia Medica and Pharmacology of Drugs Used in Allergy ETHAN ALLAN BROWN M D Tufts Medical School Boston Massachusetts
P M	<i>Special Allergies</i>
2 00 3 00	Bacterial Allergy M. SCHERAGO Professor of Bacteriology University of Kentucky Lexington, Ken- tucky
3 00 3 30	Mold Allergy Pathogenic Molds FRED W. WITTICH M D Minneapolis Minnesota
3 30 4 30	Allergy from Drug and Biological Products BRET RATNER M D New York University College of Medicine, New York New York
4 30 5 30	Physical Allergy CECIL KOHN, M D Kansas City Missouri

#### Wednesday, November 6

A M	<i>Respiratory Allergy</i>
9 00 10 00	Allergic Rhinitis FRENCH K. HANSEL M D Washington University Saint Louis Missouri
10 00 11 00	Allergic Bronchitis Bronchiectasis and Loeff- ler's Syndrome J. WARRICK THOMAS M D Graham Thomas Clinic Richmond Va
11 00 12 30	Bronchial Asthma HARRY L. ROGERS M D Jefferson Med- ical College Philadelphia Pennsylvania
12 20 1 00	Bronchoscopy in the Treatment of Asthma LOUIS CLERF M D Jefferson Medical Col- lege Philadelphia Pennsylvania
P M	<i>Respiratory Allergy (continued)</i>
2 00 3 00	Inhalation Therapy of Asthma ALVAN L. BARACH M D Columbia Uni- versity College of Physicians and Surgeons New York New York
3 00 3 45	Cardiac Asthma LEON UNGER M D Northwestern Univer- sity Medical School Chicago Illinois
3 45 4 30	Status Asthmaticus HAL DAVISON M D Emory University Atlanta Georgia

4 30 6 00	Bronchial Asthma in Infants and Children M. MURRAY PESHKIN M D Columbia University College of Physicians and Sur- geons, New York New York
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#### Thursday, November 7

A M	<i>Dermatologic Allergy</i>
9 00 10 00	Dermatologic Allergy in Children JEROME GLASER, M D University of Roch- ester Medical School Rochester New York
10 00 11 00	Atopic Dermatitis STEIHAN EPSTEIN M D, Marshfield Clinic, Marshfield Wisconsin
11 00 12 00	Contact Dermatitis RUDOLPH BAER M D New York Post Graduate Medical School of Columbia Uni- versity, New York New York
12 00 12 45	Urticaria JONATHAN FORMAN M D Ohio State Uni- versity Medical School Columbus Ohio
12 45 1 15	Poison Ivy LAWRENCE J. HALPIN M D, Cedar Rapids Iowa
P M	<i>Concurrent Laboratory and Clinical Sessions Laboratory Session—Skin tests Patch tests Passive transfer Nasal smears Molds Ex- traction methods and Standardization UNGER, HANSEL WITTICH, PRINCE HAL- PIN and ROCKWELL Pediatrics—Special problems in asthma hay fever dermatitis PESHKIN and GLASER Asthma Clinic—ROGERS UNGER DAVISON BARACH and CLERF WODEHOUSE Hay Fever Clinic—MOORE LOVELESS and Dermatology Clinic—EPSTEIN BAER FORMAN and HALPIN Neuro Allergy—MOVIES HORTON Clinic—KENNEDY CLARKE</i>

#### Friday, November 8

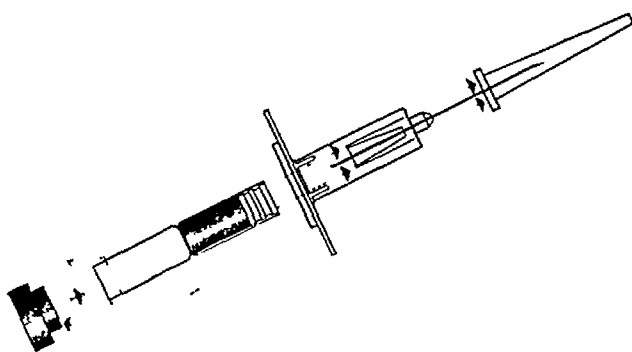
A M	<i>Hay Fever</i>
9 00 9 30	Botany ROGER WODEHOUSE Ph D Associate Di- rector of Research in Allergy Lederle Laboratories Pearl River New York
9 30 11 00	Diagnosis and Treatment of Hay Fever MERLE MOORE M D University of Ore- gon Medical School Portland Oregon
11 00 11 30	Chemical Nature of the Pollen Antigen and the Types of Extracts Used GEORGE E. ROCKWELL M D Milford Ohio
11 30 12 30	Immunology of Hay Fever Perennial and Booster Dose Therapy MARY LOVELESS M D Cornell University Medical College New York New York
12 30 1 00	Low Dosage Therapy FRENCH K. HANSEL M D Washington University Saint Louis Missouri
P M	<i>Special Allergies</i>
2 00 3 30	Food Allergy ORVAL R. WITHERS M D University of Kansas School of Medicine Kansas City Missouri
3 30 4 00	Meinere's Disease BAYARD T. HORTON M D Mayo Clinic Rochester Minnesota
4 00 4 45	Migraine FOSTER KENNEDY M D Cornell Univer- sity Medical College New York New York
4 45 5 30	Ocular Allergy A. R. RUEDEMAN M D Cleveland Clinic Cleveland Ohio
5 30 6 15	Epilepsy T. WOOD CLARKE M D Utica New York

#### Saturday, November 9

A M	<i>Special Allergies</i>
9 00 9 45	Reactions to blood transfusions and Blood Dyscrasia due to Allergy HAROLD W. JONES M D Philadelphia Pennsylvania
9 45 10 15	Joint Allergy BELA SCHICK M D New York New York
10 15 10 45	Aural Allergy HUGH KUHN M D Hammond Indiana
10 45 11 15	Common Air Molds and Their Relation to Allergy HOMER PRINCE M D Baylor University Medical School Houston Texas
11 15 11 45	Shock Therapy in Allergy GEORGE E. ROCKWELL M D Milford Ohio
11 45 1 00	Office Management HOMER PRINCE M D Baylor University Medical School Houston Texas
1 30	Luncheon Round Table Discussion

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sylvania Headquarters is at the Benjamin Franklin Hotel (For those in or just returning from military service, the  
course is \$25) Applications for the course and for hotel reservations should be placed with the Secretary American Col-  
lege of Allergists 423 La Salle Medical Building Minneapolis 2 Minnesota

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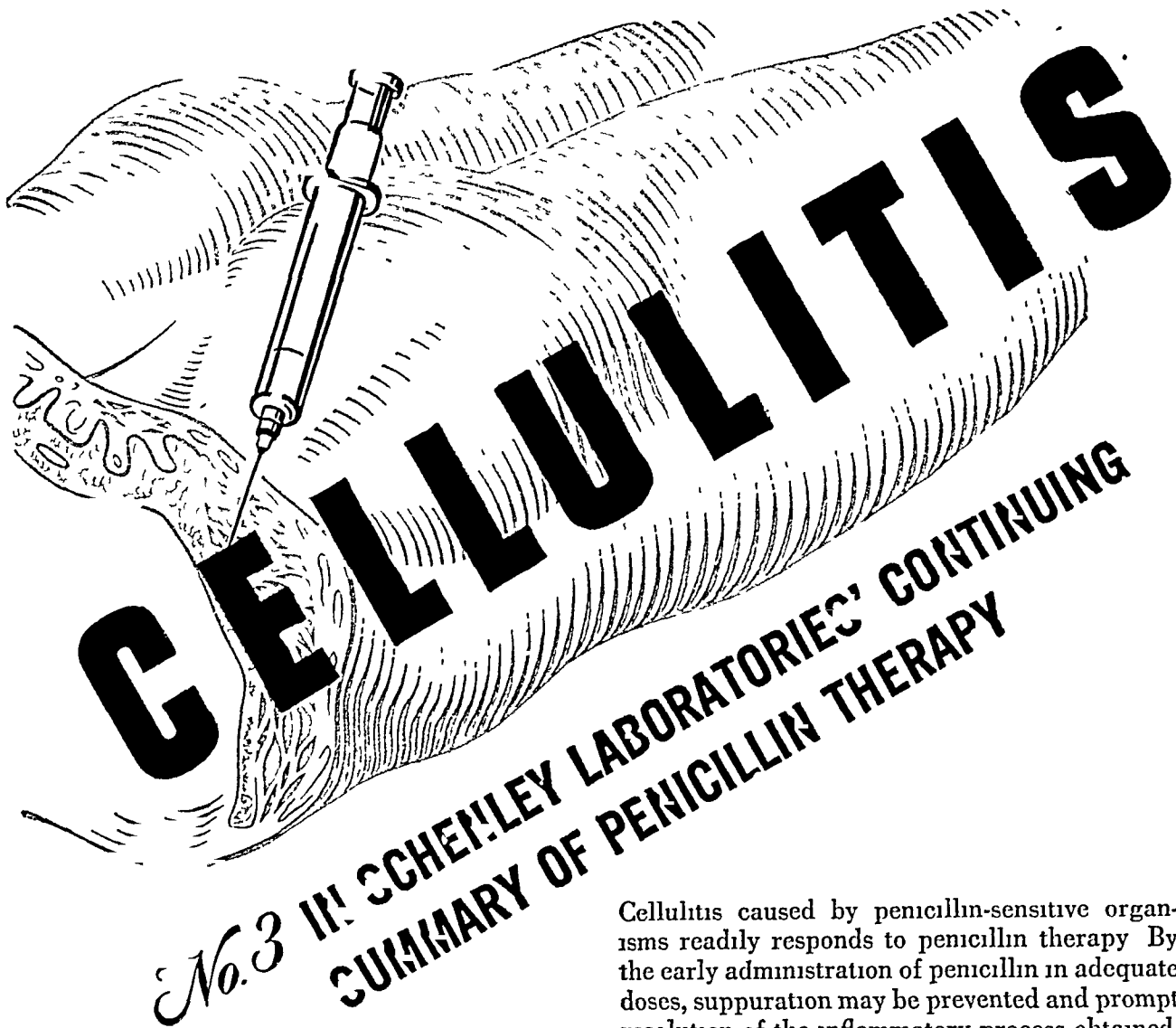
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WOLFGAST, C. F. *The Clinical Use of Penicillin. A Report of 115 Cases Treated in an Army Hospital, Texas State J. M. 40:225 (Aug.) 1944.* FARQUHARSON, R. F., GREEY, P., & TOWNSEND, S. R. *Results of Penicillin Therapy. A Report for the Joint Services Penicillin Committee, Canad. M. A. J. 53:1 (July) 1945.*

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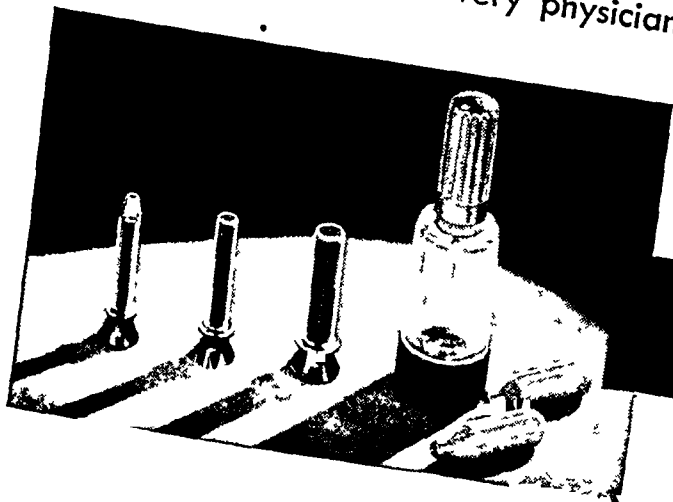
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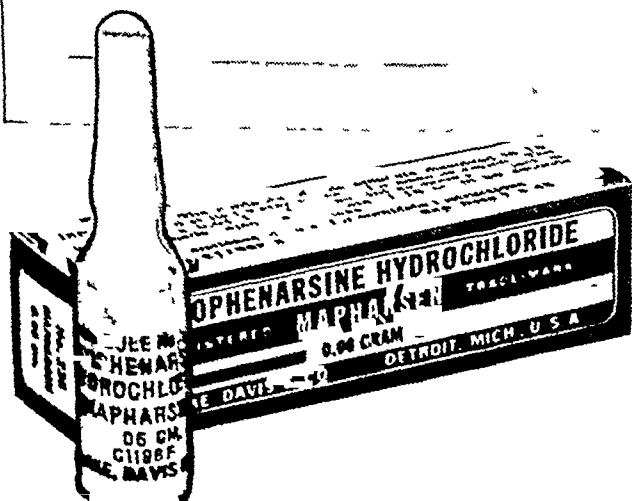
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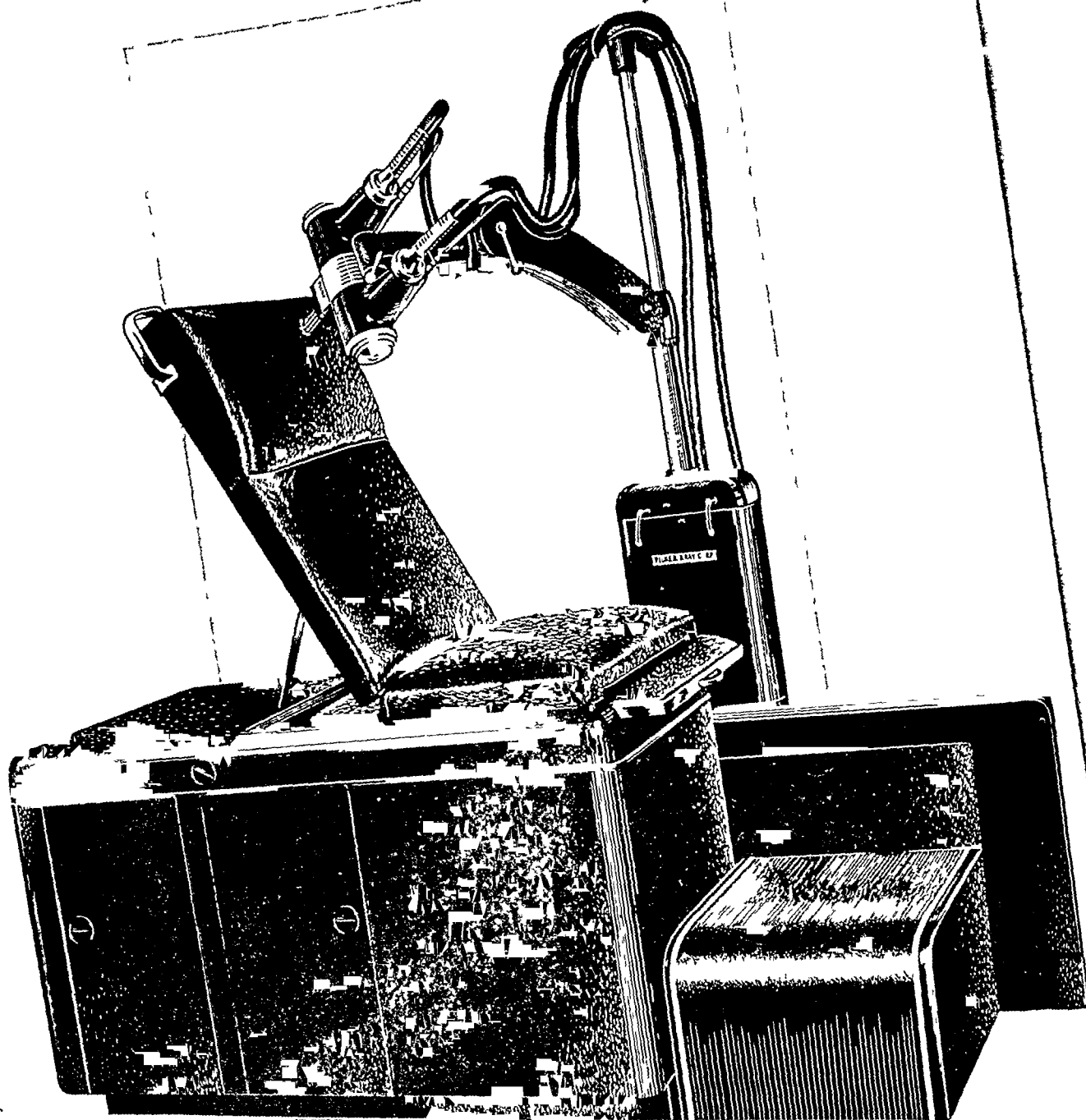
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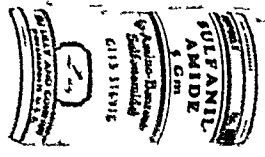
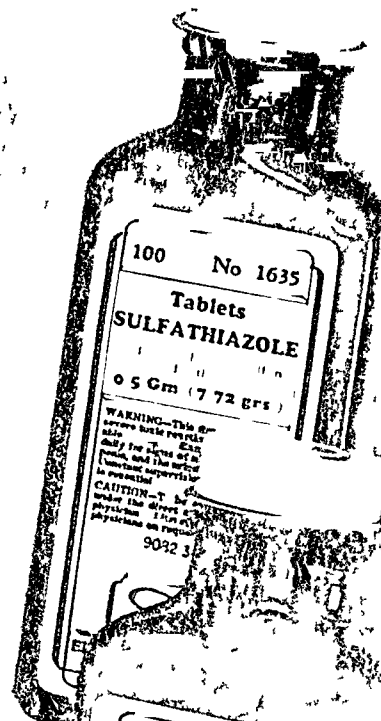
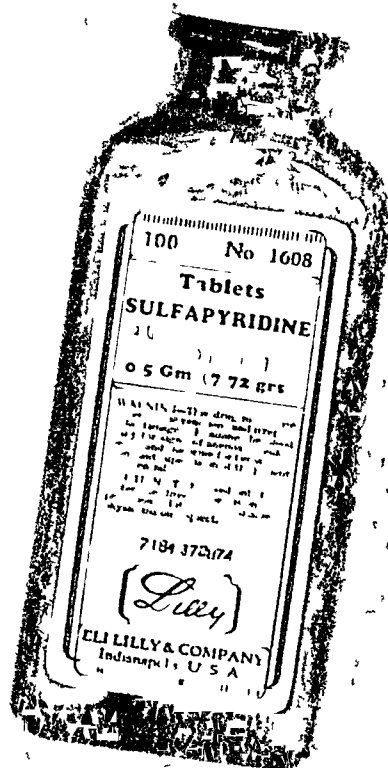
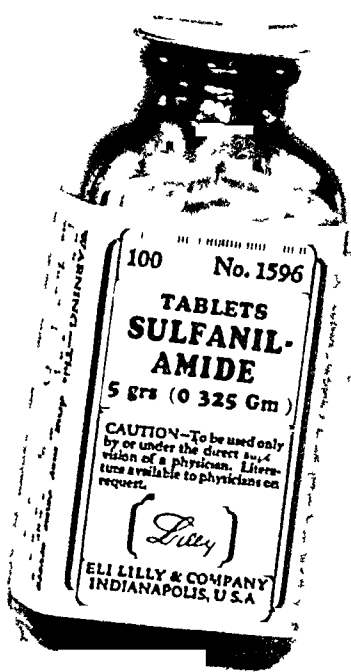


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A picture of The Good Samaritan provided the inspiration that



eventually led to the founding of Eli Lilly and Company

# Archives of Dermatology and Syphilology

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## USE OF PENICILLIN IN THE TREATMENT OF SYPHILIS IN PREGNANCY

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W. W. MURPHY, M D

DON R. PRINTZ, M D

AND

JAMES STRAUCH, M D

In Collaboration with G. W. BINKLEY, M D, SILVIO COLIMODIO, M D, J. R. DRIVER, M D,  
R. W. KILE, M D, and JOHN RAUSCHKOLB, M D  
CLEVELAND

FROM October 1943, 730 patients with early syphilis have been treated with penicillin at the University Hospitals and City Hospital in Cleveland. In addition, a number of patients with syphilis of the central nervous system have been treated, but these cases have not been incorporated in this report. Moreover, many of these patients have been retreated since and a good many a second time, with progressively larger doses of penicillin as indications warranted.

From the Department of Dermatology and Syphilology, Western Reserve University School of Medicine, and of the City Hospital and University Hospitals, H. N. Cole, Director

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Western Reserve University School of Medicine.

The results which have been presented in this paper must be interpreted in the light of the fact that from June 1943, the date of inception of the study, to the present commercial penicillin has been a changing mixture of various substances. The content of "impurities" has gradually decreased as potency, in terms of units per milligram, has increased. The relative amounts of the several identified penicillin fractions C, F, X and K, have likewise varied from time to time. Those two changes, and perhaps others, suggest that therapeutic efficacy may not have remained constant and that it may be significantly different today than it was originally. It is not now possible to assess the extent to which these changes may have affected the results here reported.

## ROUTINE IN USE OF PENICILLIN

All the patients studied were given careful physical examinations on admission and thereafter as indicated. With any open lesions, dark field examinations were made every few hours at first—as many as were necessary to study the disappearance of treponemas. Serologic examinations of the blood were made frequently.

At the University Hospital progressive dilutions are made on serums showing a reading of 1 plus on the Kline diagnostic test and 3 plus or more on the Kline exclusion test. Dilutions commence with 1:10, and the end point is the positive reading of "2 plus" or more. The technic used at the City Hospital is a centrifuged resuspension technic, with use of the Kline exclusion antigen, and is read grossly<sup>1</sup>. The titers are reported by progressive dilution from 1:1. The two methods give approximately parallel results. For example 1:16 by the latter technic is about 1:10 or 1:20 by the former. Two hundred and fifty quantitative tests were run in parallel with the Lund technic. It was found that the reciprocal of the titer was about four times the Kahn unit. So for conversion the titer is divided by 4, thus 1:32 would equal 8 Kahn units. Roughly 4 units of City Hospital or 4 units of Lakeside Hospital correspond to 1 Kahn unit.

Lumbar punctures were made on all the patients, and if the fluid gave a positive reaction they were repeated on the dismissal of the patient and thereafter, if possible, every three months. As nearly as was possible serologic examinations were also made every two to three months or oftener after dismissal. An attempt has constantly been made to employ a titrated serologic test, as this gives better indication of the patient's response to treatment. A small rise or fall in the titer may mean nothing, and it may vary from week to week. It is the direction of the titer and the rises or falls in titer that have significance. A persistent titer—perhaps at 1:64 (16 Kahn units)—indicates that the patient will bear watching, perhaps a lumbar puncture is indicated, and certainly a careful physical examination is in order. In early syphilis, in which it has continued over three to four months, retreatment with double the first dose of penicillin is necessary.

## RESPONSE TO TREATMENT

Acute mucocutaneous lesions of syphilis respond rapidly to penicillin therapy and may clear up entirely in one to three weeks, depending on their severity.

Dark field examinations of open genital lesions ordinarily show a change to negative in from twelve to eighteen hours—rarely longer if large enough doses of penicillin are employed. In cases of positive reactions to serologic tests, the response to treatment is slower, particularly in secondary syphilis. After institution of therapy the titer may rise for a week or more, perhaps from 1:64 to 1:128 (16 to 32 Kahn units) and then gradually drop to negativity. This may require from four to eight or twelve weeks. The direction of the titration curve is a good indication of the patient's response to treatment. A serologic

1 Lund, H. Titration of Traces of Reagin. Technique of Flocculation Using Maximal Serum Proportions with Secondary Recovery of Antigen, *Am J Syph, Gonorr & Ven Dis* 26 1-15 (Jan) 1942.

titer that has become completely negative and then once more resumes a positive phase bears watching

With lumbar punctures, a cell count is made and also an estimation of the total protein content, Pandy and Nonne tests, colloidal gold or gum mastic tests and finally a Wassermann test in ascending amounts of fluid at least 0.1, 0.5 and 1.0 cc

#### RESUME OF THE GROUPS TREATED

Thirty-one patients have been treated with a dosage of 60,000 units of sodium penicillin, 1,000 units intramuscularly every three hours for a total of sixty doses in seven and one-half days. In 13 of these patients the treatments have been failures, there being neurorelapses in 5 of them, serologic and clinical relapses in 2 and serorelapses in 6. Moreover, of the remaining patients there has been no check-up in over three months on 15 of them. Two are serologically and clinically well less than one year and 1 over one year afterward.

Forty-seven patients were treated with 60,000 units, administered as in the foregoing group, plus an intravenous injection of oxophenarsine hydrochloride, 0.040 Gm every other day for a total of 0.320 Gm. There has been no check-up on 22 of these patients in over three months. Four are serologically and clinically well less than one year and 4 over one year afterward. There have been 16 cases of failure of treatment: 10 of serologic and clinical relapse, 2 of relapse of syphilis of the central nervous system, 3 of serorelapse alone and 1 of clinical relapse, the serologic reaction having never changed.

Eighty-one patients received 300,000 units intramuscularly, 5,000 units every three hours for seven and one-half days. Forty-two of these patients have not been contacted in over three months, 4 are serologically and clinically well less than one year and 8 over one year afterward. There have been 26 cases of failure of treatment: 10 of serorelapse, 9 of serologic and clinical relapse, 5 of relapse of syphilis of the central nervous system and 2 of clinical relapse, with no change in the positive reactions of the blood.

With a dosage of 1,200,000 units, 20,000 every three hours for seven and one-half days, only 9 patients were treated that are included in this report. There is an interval since the last check-up of over three months for 2 of them. Two are seronegative and clinically well less than one year and 1 over one year afterward. Two patients have had serorelapses. One further patient with neurorelapse from 60,000 units was retreated with this dosage, relapsed again and retreated with 9,000,000 units. Consequently, the patient will not be considered in this group.

A further group of 129 patients was treated with this same total dosage: 40,000 units being given every six hours instead of every



three hours for seven and one-half days. The interval since the last check-up was more than three months in 55 of the cases. Twenty-six are serologically and clinically well less than one year and 15 over one year afterward. There have been 10 cases of serorelapse only, 12 of serologic and clinical relapse and 1 of clinical relapse only, with no change in the positive serologic reaction.

With a dosage of 1,600,000 units, 20,000 every three hours for ten days, 369 patients have been treated. Ninety-nine patients have had an interval since the last check-up of more than three months. Sixty-nine are seronegative and clinically well less than one year afterward, but none for more than a year, as this is one of the more recent groups to be treated. There have been 18 cases of serorelapse and 9 of serologic and clinical relapse, or a total of 27 cases of failure thus far. There are pending 174 patients with no neurorelapses as yet.

Fifty-four patients have been treated with a dosage of 2,400,000 units, 20,000 units every three hours for fifteen days. Seventeen of them have not been checked for the past three months. Sixteen are serologically and clinically well less than one year afterward and there have been 2 cases of relapse, a serorelapse and clinical type and a clinical relapse only, with no change in the positive serologic reaction.

The first patients treated were a group of 5 men to whom, on the suggestion of Prof. J. T. Weain, 400,000 units were given by intravenous drip the first two days and the remaining 800,000 units in intramuscular injections of 20,000 units every three hours for five days. A like group of 5 women was given 20,000 units intramuscularly every three hours for seven and one-half days, for a total of 1,200,000 units. Three of this entire group have been well for one year or longer and 1 for over two years, 6 have lost contact.

#### REACTION FROM PENICILLIN

Several batches of penicillin from a particular manufacturer caused the patients to complain bitterly of burning and pain locally after the intramuscular injection. Occasionally, otherwise, a patient may make this complaint, but ordinarily not. Again, if injections are given every two hours it may sometimes be necessary to use areas other than the buttocks for the injections. Herxheimer reactions, with accentuation of the eruption, are the rule after the first injection and will be accompanied with a febrile reaction, the temperature often reaching 38 or 39 C and occasionally higher. It regresses as a rule in a matter of hours. Along with this reaction herpes labialis occasionally occurs. Urticaria is encountered now and then, and rarely an obstinate giant urticaria will appear along toward the end of the penicillin therapy or afterward and last for several weeks. Occasionally an erythema multiforme type of eruption on the extremities and even the trunk may show

up, but generally it does not last. Several cases of an erythema nodosum-like eruption on the shins was noted. Contrary to results with other antisyphilitic remedies, severe reactions from penicillin did not occur.

Nevertheless, due to the acute Herxheimer type of reaction with the first injections, the possible dangers of too quick use of this drug in cardiovascular syphilis and in gummatous lesions of the liver and of the central nervous system should be seriously considered. Preliminary treatment with a heavy metal might well be in order to obviate too rapid healing, with scar formation and production of harmful contractions in delicate structures in such late cases.

#### SYPHILIS AND PREGNANCY

Since the inception of this study on the use of penicillin in the treatment of syphilis, among 730 cases 47 pregnant syphilitic patients have been handled. In 2 of the cases now pending, a second pregnancy has supervened since treatment was originally given. The cases are originally included, but the second pregnancy and 5 cases in which the children have not yet been born are not included.

*Dosage of Penicillin Employed* When this study was started on plans of the Penicillin Panel of the Subcommittee on Venereal Diseases, National Research Council, only small doses were employed and 3 of the prospective mothers received but 60,000 units, 1,000 every three hours for seven and one-half days. In 1 instance, with the therapy received in the seventh month of pregnancy, the child four months after birth showed a completely negative reaction to the Kline diagnostic and exclusion and Lund-Wassermann titration tests. There are no further data on the mother. In the second case, that of a mother with condyloma lata who received treatment in the eighth month of pregnancy, the child four months after birth has exactly the same negative serologic picture. Unfortunately, in acute syphilis treated with 60,000 units there have been far too many relapses.

In Rosabelle G., three months pregnant and suffering from a generalized eruption and moist papules, a seroclinical relapse occurred just before delivery and she was given 1,200,000 units of sodium penicillin, of which approximately 1,000,000 units was received before the birth of the child and 200,000 units after the birth had taken place, there being no interruption in the intramuscular injections of 20,000 units every three hours for seven and one-half days. The child was delivered May 1, 1944. The following results were obtained on subsequent check-ups:

	Kline Diagnostic	Kline Exclusion	Wassermann (Lund Technic)	Titer
5/ 3/44	++++	++++	++++	1 16 (4 Kahn units)
7/10/44	—	+	—	
12/14/44	—	—	—	
7/26/45	—	—	—	

The mother continued to show a negative reaction up to Sept 5, 1944, when she again had a seroclinical relapse. (The titer rose from 1 4 [1 Kahn unit]

July 15 to 1 64 [16 Kahn units] September 5) She is now on routine heavy metal therapy, refusing to enter the hospital for further treatment with penicillin

In 3 cases a dosage of 300,000 units, 5,000 every three hours for seven and one-half days, was given In 6 cases a dosage of 1,200,000 units was employed, in 7 cases 1,600,000 units, in 1 case 2,000,000 units and in 22 cases 2,400,000 units

In a single instance there was used a dosage of 60,000 units of penicillin intramuscularly, with the technic we have outlined, plus oxophenarsine hydrochloride given intravenously, 0.04 Gm every other day for a total of 0.320 Gm This child has been seronegative and completely well for nine months

*Dosage Relation of Penicillin to Relapses*—Perhaps a review of the various dosages of penicillin employed and sequelae in the child may help in estimation of the proper dosage in pregnancy complicated by syphilis

Three patients on a dosage of 60,000 units are hardly enough for statistical evaluation, and in 1 of these there was severe relapse in the mother The general experience with 60,000 units in acute syphilis is that sooner or later there will be a relapse Even with 300,000 units there was a relapse in the form of early congenital syphilis

Virginia L., seven months pregnant and suffering from early syphilis, was given 5,000 units of penicillin every three hours for seven and one-half days Her serologic reactions were as follows

	Kline Diagnostic	Kline Exclusion	Wassermann (Lund Technic)	Titer
5/10/44	++++	++++	—	1 6 (1½ Kahn units)
11/ 4/44	+	++++	++++	1 8 (2 Kahn units)
1/ 2/45	+	+	++++	
1/30/45	+	+	—	

The child was delivered June 8, 1944, and its serologic titers from June 24 to August 21 continued strongly positive, the last showing 1 256 (64 Kahn units) At this point, in addition, a mucocutaneous eruption developed in the child and lumbar puncture revealed 112 cells (98 mononuclears and 14 polymorphonuclears) and spinal fluid gave a 4 plus Pandy and a 4 plus Wassermann reaction in 0.1, 0.5 and 10 cc—in other words, there were a mucocutaneous relapse and acute meningeal syphilis The baby was given 600,000 units of sodium penicillin, 10,000 units intramuscularly every three hours for seven and one-half days, from August 15 to August 22 Her reactions in follow-up serologic examinations have been as follows

	Kline Diagnostic	Kline Exclusion	Wassermann (Lund Technic)	Titer
9/ 7/44	++++	++++	++++	1 128 (32 Kahn units)
11/ 7/44	++++	++++	++++	
2/15/45	—	+	+	1 2 (½ Kahn unit)

This case, unfortunately, has not been checked since but well illustrates that a higher dosage of penicillin is preferable for treatment of pregnant syphilitic patients

Nine patients were treated with 1,200,000 units, and there are no relapses thus far

Eight patients were treated with 1,600 000 units, and 1 relapse occurred

A woman pregnant two months was treated February 12 to February 27, 1945. A seroclinical relapse developed late in August 1945 and showed a titer of 1:256 (64 K $\ddot{a}$ hn units), and the patient was given 2,400,000 units of penicillin from August 30 to September 15. Twins were born September 20 and on October 27 showed the following reactions

	Kline Diagnostic	Kline Exclusion	Wassermann
Barbara	++	++++	++
William	++	++++	—

These serologic reactions even yet present in part the maternal serologic reactions and will require further investigation

But 1 patient has had a dosage of 2 000 000 units

A mother, Norma W., with a maculopapular syphiloderm received 400,000 units of penicillin (July 8 to July 12, 1945) before the premature delivery of a child, the remainder, 1,600,000 units, was given July 12 to July 22. The child's reaction to a serologic test on September 6 was completely negative. The babe at premature delivery showed no clinical evidence of congenital syphilis. The premature birth was not due to the penicillin and it is felt that it was due to the syphilis. Certainly the child shows no evidence of the disease.

The outcome here will be most interesting and shows the great value of penicillin in acute syphilis even up to the time of delivery. It is never too late to use it, though its early use is preferable.

Seventeen patients have been treated with a dosage of 2,400,000 units. In 1 patient with early latent syphilis, five months pregnant and showing strongly positive serologic reactions with a titer of 1:64 (16 K $\ddot{a}$ hn units), the penicillin was given from March 29 to April 14, 1945. The child was born April 27, showing no evidence of syphilis. The serologic reaction of the mother on October 11 still showed a titer of 1:16 (4 K $\ddot{a}$ hn units), which is not unusual in latent syphilis. In still another patient Lucille W., eight months pregnant and with early latent syphilis (titer 1:16 [4 K $\ddot{a}$ hn units]), treatment was administered Oct 30 to Nov 10, 1944. There was a stillbirth in the home on Jan 14, 1945, with no opportunity to investigate the fetus.

In still another patient receiving 2,400,000 units prior to conception, there occurred the birth of a macerated fetus at seven months, two hundred and forty-seven days after treatment. Unfortunately, no examination of the fetus was made.

There are 2 cases of seropersistence in the child, 5 children with no data available and 7 patients showing completely negative serologic tests for one, two and one-half, three, three, three, four and five months respectively.

The largest dosages of penicillin have been the last employed in point of time in this investigation, hence the shorter opportunity of evaluating

their effects. Is it not interesting that in the one woman receiving 60,000 units plus oxophenarsine hydrochloride, 0.04 Gm intravenously every other day for a total of 0.32 Gm, the child has remained clinically and serologically cured, apparently, for nine months?

*Reactions from Penicillin Used in the Treatment of Syphilis in Pregnancy*—No unforeseen complications have arisen outside of the usual Herxheimer reaction seen in acute syphilis. It is characterized by a sharp rise in temperature for a few hours after the injection and in an accentuation of the lesions of the skin and mucous membrane. The two premature births were certainly not due to the penicillin, and one of them was certainly not due to the syphilis. Nor could the stillbirth be blamed on the penicillin. Unfortunately one occurred in the home, and there was no opportunity for check-up. The macerated fetus at 7 months may have been syphilitic, and the premature birth was not due to penicillin.

#### COMMENT

Syphilis in pregnancy is apparently one of the ideal situations for the use of penicillin. There are no severe reactions with which to contend. There is not the great danger of miscarriage or premature birth, never any damage to the unborn child from the drug employed and no danger of hemorrhagic encephalitis in the mother. As to the dosage indicated, it is shown that even with an abnormally small dose like 60,000 units, 1,000 units every three hours for a total of sixty doses in seven and one-half days, the child may be born free from syphilis. However, with such small doses there is ever the danger of relapse on the part of the mother, certainly more than 50 per cent, and it is advisable to employ larger doses of at least 2,400,000 units, 20,000 units every three hours, day and night, for fifteen days. Probably further study will even show the value of a higher dosage or perhaps given in a shorter period, for certainly the physician should run no risk of relapse in his patient and of possible infection of the unborn child. There is a further great advantage of the penicillin over heavy metal therapy. While it is well to administer therapy as early as possible, yet with penicillin treatment successful results are possible even up to termination of the pregnancy as was found in the case of Rosabelle G., already mentioned, who received 1,000,000 units of her full 1,200,000 units before the child was born and whose child at last report was clinically well and serologically negative. The mother, even in the last month of pregnancy, if the child is viable may be treated, and the child's syphilis will also be treated, with, as has been shown, successful results, just before birth. This was not possible with heavy metal therapy. In fact, the syphilologist formerly felt that progressively after the fourth month of pregnancy cure was to be expected less and less—the child would perhaps be viable but still have syphilis.

*Role of the Titrated Serums in the Pregnant Syphilitic Patient*

It is particularly necessary that the syphilitic prospective mother and her child be carefully followed not only clinically but also serologically. Under ideal conditions the titrated test of the blood of the prospective mother should be taken every two months and that of the child at every two months after birth for the first six months and then every three months until the serologic reaction has been completely negative for one year. With the treated mother showing a persistent titer or a real persistent increase in titer, the question of retreatment with a double dose of penicillin arises. A single rise from 4 Kahn units to 16 is not sufficient, perhaps the next month it will drop back to 4 or even to negativity. It is the persistent rise that has significance and should cause the physician to consider further treatment. In the child, a positive reaction to a serologic test for syphilis at birth may simply mean a reflection of the mother's serologic reaction. After the second or third month this is no longer true, and if such a child has not only a positive serologic reaction but also a persistent rise in titer, perhaps along with clinical symptoms, then the problem of retreatment arises. The titrated serum is a necessity in the handling of the pregnant syphilitic woman and of her child.

*Effects of Penicillin on the Syphilitic Mother* Among the 42 mothers the data reveal that seropersistence has continued since the birth of the child in 1 instance for eight months. The mother was three months pregnant and was given 1,200,000 units of penicillin over a period of seven and one-half days. While she shows no evidence of syphilis outside of the positive serologic reaction, there is a titration report of 1:128 (32 Kahn units) at the end of eight months post partum. This patient should be carefully rechecked, a lumbar puncture should be made and, even if the reaction of the fluid should be negative, she should be retreated with a double dose of penicillin (2,400,000 units). In 5 other mothers there is a seropersistence. In 7 the titer is falling and requires further follow-up. In 4 instances there have been relapses as already mentioned: 1 after a dose of 60,000 units, 1 after 1,200,000 units (retreatment of 60,000 units), 1 after 1,600,000 units and 1, in the form of a macerated fetus, possibly syphilitic, born at the seventh month, after 2,400,000 units. Unfortunately, no data are available for 10 mothers. Fifteen of the mothers are apparently well, and they show completely negative serologic reactions: 3 after 300,000 units, 9 after 1,200,000 units, 1 after 1,600,000 units and 2 after 2,400,000 units respectively.

SUMMARY

1. A report is made on 730 patients with early syphilis treated with sodium penicillin in varying dosages as outlined by the Penicillin Panel of the Subcommittee on Venereal Diseases, National Research Council.

2 The drug in all but 5 cases was administered by the intramuscular route and generally every three hours

3 No severe reactions are noted after the use of the drug, occasionally there is some local discomfort and now and then a giant urticaria

4 *Treponema pallidum* generally disappear from local lesions in a matter of ten to fifteen hours, and lesions of syphilis heal in a period of one to two or three weeks, depending on their severity

5 Serologic reactions are slower in their response. Emphasis is laid on the use of the titrated serums in all cases of this form of treatment. Often the titer will temporarily rise and then gradually fall to negativity in a matter of several months, depending on the stage of the disease and on the dosage employed

6 Relapses are seen and will be discussed in a succeeding paper

7 Among 730 cases there were 47 pregnant syphilitic patients treated

8 Syphilis in pregnancy is an ideal situation in which to use penicillin, because of absence of severe reactions and, further, because the drug may be used successfully even late in the pregnancy, provided the child is still viable

9 There were 1 child born with congenital syphilis and syphilitic meningitis and 1 macerated fetus born at 7 months. The mother in the first instance was on a low dosage schedule of penicillin and the macerated fetus ensued after 2,400,000 units

10 The dosage schedule for the treatment of early syphilis is still in the formative stage and requires further careful study. Certainly the patient should receive at least 2,400,000 units and perhaps even more

## CHROMOBLASTOMYCOSIS

Report of Two New Cases Observed in the Isthmus of Panama

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TWO NEW cases of chromoblastomycosis are reported in this paper to make a total of 3 cases already diagnosed in the Isthmus of Panama and a total of 154 cases diagnosed in the whole world<sup>1</sup> since the discovery of the disease by Pedroso and Gomez<sup>2</sup> in Brazil and the first publications by Medlar<sup>3</sup> and Lane<sup>4</sup>

I am not able to tell anything about the incidence of the disease here until the medical profession has a better knowledge of its five clinical forms,<sup>5</sup> and of how a diagnosis may be made. Chromoblastomycosis may be diagnosed by the observation of sclerotic cells on microscopic examination of the material obtained by scraping the lesions, by the culture of the scabs in Sabouraud's medium and the subsequent

From the medical department of the Hospital Santo Tomas

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2 Pedroso, A, and Gomez, J M Sobre cuatro casos de dermatite verrucosa produzida pela Phialophora Verrucosa, Ann paulist de med e cir **9** 53 (March) 1920

3 Medlar, E M (a) A Cutaneous Infection Caused by a New Fungus, Phialophora Verrucosa, with a Study of the Fungus, J M Research **32** 507 (July) 1915, (b) A New Fungus Phialophora Verrucosa, Pathogenic for Man, Mycologia **7** 200, 1915

4 Lane C G A Cutaneous Lesion Caused by a New Fungus (Phialophora Verrucosa) J Cutan Dis **33** 840 (Dec) 1915

5 Sabouraud, R Maladies du cuir chevelu III Les teignes, Paris, Masson & Cie, 1910, p 105



study of the fungi<sup>6</sup> or by the agglutination reaction<sup>7</sup>. However, it was a great surprise to me, when initiating the study of this chapter of mycology under Professor Carrion at the School of Tropical Medicine in Puerto Rico, to learn that there had not been a single case of chromoblastomycosis reported in the Isthmus of Panama, although the literature showed that it had been recognized in other Central American countries, like Guatemala<sup>8</sup> and Costa Rica<sup>9</sup> (the country to the north of the Isthmus), and in the Caribbean Zone (also adjacent to us), where over 50 cases were reported since 1933<sup>10</sup>.

6 (a) Brumpt, E. *Precis de parasitologie*, ed 3, Paris, Masson & Cie, 1922, p 1105. (b) Carrion, A. L., and Emmons, C. W. A Spore Form Common to Three Etiologic Agents of Chromoblastomycosis, *Puerto Rico J. Pub. Health & Trop. Med.* **11** 114 (Sept.) 1935. (c) Negroni, P. Estudio micologico del primer caso argentino de cromomycosis *Fonsecaea (n. g.) pedrosoi* (Brumpt, 1921), *Rev. d. Inst. bact.* **7** 419 (March) 1936. (d) Dodge, C. W. *Medical Mycology. Fungous Diseases of Men and Other Animals*, St. Louis, C. V. Mosby Company, 1935, p 850. (e) Emmons, C. W., and Carrion, A. L. *Hormodendrum Pedrosoi*. An Etiological Agent in Chromoblastomycosis, *Puerto Rico J. Pub. Health & Trop. Med.* **11** 639 (June) 1936. (f) The *Phialophora* Type of Sporulation in *Hormodendrum Pedrosoi* and *Hormodendrum Compactum*, *ibid.* **11** 703 (June) 1936. (g) Moore, M. The Organisms of Chromomycosis of North and South America, *Science* **83** 603 (June 19) 1936. (h) Carrion, A. L. Chromoblastomycosis. A New Clinical Type Caused by *Hormodendrum Compactum*, *Puerto Rico J. Pub. Health & Trop. Med.* **11** 663 (June) 1936. (i) Martin, D. S., Baker, R. D., and Conant, N. F. A Case of Verrucous Dermatitis Caused by *Hormodendrum Pedrosoi* (Chromoblastomycosis) in North Carolina, *Am. J. Trop. Med.* **16** 593 (Sept.) 1936. (j) Moore, M., and de Almeida, F. P. New Organisms of Chromoblastomycosis, *Ann. Missouri Bot. Gardens* **23** 543 (Nov.) 1936. (k) Emmons, C. W., and Carrion, A. L. Sporulation of the *Phialophora* Type in *Hormodendrum*, *Mycologia* **29** 327 (May-June) 1937. (l) Carrion, A. L. The Specific Fungi of Chromoblastomycosis, *Puerto Rico J. Pub. Health & Trop. Med.* **15** 340 (June) 1940. (m) Chromoblastomycosis, *Mycologia* **34** 424 (July-Aug.) 1942. (n) Conant, N. F., Martin, D. S., Smith, D. T., Baker, R. D., and Callaway, J. L. *Manual of Clinical Mycology*, Military Medical Manual, National Research Council, Division of Medical Sciences, Philadelphia, W. B. Saunders Company, 1944.

7 Conant, N. F., and Martin, D. S. The Morphologic and Serologic Relationships of the Various Fungi Causing Dermatitis Verrucosa (Chromoblastomycosis), *Am. J. Trop. Med.* **17** 553 (July) 1937.

8 Morales, R., cited by Conant and Martin.<sup>7</sup>

9 (a) Salisbury, E. Y. Mossy Foot. A Case Report in Seventeenth Annual Report of the Medical Department of the United Fruit Company, Boston, 1928, p 185. (b) Nauck, E. G. Histologische Untersuchung über Dermatitis verrucosa und Mossy-Foot, *Arch. f. Schiffs- u. Tropen-Hyg.* **35** 394 (July) 1931. (c) Rotter, W., and Peña Chavarria, A. Untersuchungen über Blastomykosen in Costa Rica, *ibid.* **37** 1 (Jan.) 1933. (d) Weitere Untersuchungen über Blastomykosen in Costa Rica, *ibid.* **38** 406 (Oct.) 1934.

The first case encountered and diagnosed in this hospital revived in my mind what I had already said about the probable existence of the disease in this country, but it was not actually the first case, for in the course of the last two years Dr Wedding, in collaboration with Dr Snow and Dr Tomlinson,<sup>1g</sup> had already diagnosed the first case of the disease in the Isthmus of Panama

#### REPORT OF CASES

CASE 1—L C, a married white man 49 years old, was admitted to the Santo Tomas Hospital on July 28, 1944. He was a native of Rio de Jesus, where

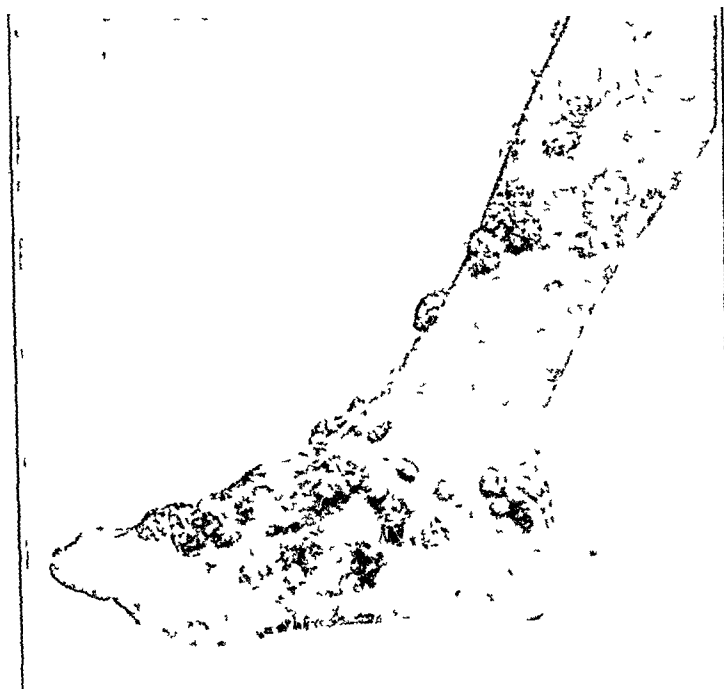


Fig 1 (case 1)—Moderate elephantiasis of the right leg, with multiple verrucous formations. On the medial aspect of the middle third of the leg is an oval scar surrounded by the same kind of verrucous formation. The largest lesion is located on the dorsum of the foot.

10 (a) Hoffmann, W H. La cromoblastomycosis en Cuba y la enfermedad de Guiteras o "chappa," *Rev méd cubana* **39** 420 (April) 1928. (b) O'Daly, J A cited by Carrion<sup>6b</sup>. (c) Carrion, A L, and Koppisch, E. Observations on Dermatomyosis in Puerto Rico. Report on a Case of Chromoblastomycosis, Puerto Rico J Pub Health & Trop Med **9** 169 (Dec) 1933. (d) Carrion, A L. Chromoblastomycosis. Preliminary Report on a New Clinical Type of the Disease Caused by *Hormodendrum Compactum*, nov sp, *ibid* **10** 543 (June) 1935, (e) Chromoblastomycosis in Puerto Rico, *ibid* **14** 37 (Sept) 1938. (f) Carrion, A L, and Pimentel-Imbert, M F. Chromoblastomycosis in the Dominican Republic, *ibid* **13** 522 (June) 1938. (g) Wilson, S J, Hulsey, S, and Weidman, F D. Chromoblastomycosis in Texas, *Arch Dermat & Syph* **27** 107 (Jan) 1933. Pardo-Castello and others<sup>1b</sup>. Pozo-García,<sup>1f</sup> Morales<sup>8</sup> Salisbury<sup>3a</sup> Nauck<sup>9b</sup> Rotter<sup>9c,d</sup>

he lived and worked (without shoes) as a farmer until the day he was hospitalized with the elephantiasis-like aspect and nodules of superficial wartlike appearance on his right leg (fig 1) from the lower third of the thigh to the sole. The first lesion, which had appeared eight and a half years previously and measured 11.25 by 7.5 cm., was the largest and was located on the dorsal surface of the right foot. The second, which had appeared three years later, was located in the angle of flexion of the foot. The others, which had appeared within the last fifteen months, covered the dorsum, sides and sole, both malleoli, around and back of the malleoli and the region of the tendo Achillis, lesions were also on the right leg, knee and lower third of the internal surface of the thigh. The largest measured 11.25 by 6.25 cm and was located about the internal lower third surface of the thigh, the smallest lesions were located on the sole and plantar arch and were the size of the head of a common pin.

The patient did not remember having received any injury at the location of the first lesion and described the beginning and development of the eruption by saying that each prominent nodule appeared first as a small papillomatous formation the size of a pinhead. It grew slowly, with a tendency to confluence and to the formation of larger warty nodules. The largest of these had the appearance of a cauliflower and was located about the dorsum of the foot. Every one of these warty nodules had a well defined border, was painless, pruritic, firm and occasionally hard. It was superficially covered by gray scales, more or less adherent or by dirty dark, scabs, when these scales or scabs were scraped off there was a tendency to bleed easily and to expel small quantities of whitish masses or, occasionally, of yellow, purulent masses with a characteristic penetrating odor. I saw, moreover, that the first lesion (on the dorsum of the right foot) and one of the later lesions (on the posterior surface of the leg) presented an area of spontaneous healing which exposed what seemed to be a white scar of retraction surrounded by a ring of warty growths.

The patient denied having received medical treatment, except for the chemical cauterization of some of the warty formations with copper sulfate at the beginning of his hospitalization, before a definite cause had been established.

*Family History*—The information received was essentially noncontributory except that the patient had three sons with jaws.

*Past Clinical History*—The patient had malaria on two occasions, pleurisy on the right side, intestinal parasites and congestive cardiac failure.

*Physical Examination and General Diagnosis*—The patient was 164 cm in height, 54 Kg in weight, white and pale, and resting quietly in bed. Besides the warty lesions just described and the elephantiasis-like appearance of the right leg, he presented (a) internal bilateral pterigium, (b) chronic granulosis of the pharynx, (c) alveolar pyorrhea, (d) pleurisy on the right side in the process of resolution and (e) chronic splenomegaly of malarial origin.

*Laboratory Data*—The results of laboratory examinations were as follows: (a) Microcytic hypochromic anemia was reported. (b) Intestinal parasites (eggs of *Uncinaria* and *Trichuris trichiura*) were present. (c) Receded elephantiasis and arteriosclerosis of the right lower limb without any bone change were shown by roentgenograms. (d) The mycotic nature of the warty lesions was observed on microscopic examination of the material scraped from the surface of the warty nodules after it had been treated with 95 per cent alcohol and 20 per cent potassium hydroxide. In the slides prepared for that purpose (fig 2) I found abundant sclerotic cells 7 to 30 microns in diameter, isolated or in groups, round,

enlarged or polyhedral, of a color between clear yellow and dark brown and always with a double contour. They frequently had a central septum and outlined divisions and had hyphae emerging from them. The hyphae were either with or without chlamydospores and had what appeared to be dichotomic segmentation such as one is accustomed to see in the *Hormodendrum* type of sporulation.

CASE 2—J. R. N., a white man 48 years old, was admitted to the Santo Tomas Hospital on Nov. 1, 1944. He was born and raised in Chitre where he lived and worked as a farmer until the day of his hospitalization.

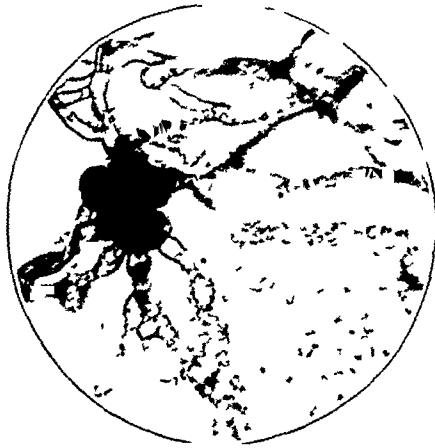


Fig. 2 (case 2)—A cluster of sclerotic cells from crusts, showing the thick wall from which emerge a number of hyphae with round formations like chlamydospores,  $\times 970$ .



Fig. 3 (case 2)—Multiple verrucous formations are seen on the dorsum of the left hand, with the oldest and largest lesion on the index finger. Several small lesions are present on the lower half of the forearm.

The lesions on the left arm were wartlike in appearance and had been developing over a period of two and a half years. The one on the back of his left index finger (fig. 3), the oldest, measured 5 by 4 cm. The other lesions, of more recent appearance, occurred with the history of an open wound preceding them, progressed gradually and measured 1.5 by 1 cm to 4.5 by 4 cm. They

were located on the dorsal surface of the rest of his left fingers and hand and over the external surface of the left forearm up to the elbow

He said that each warty mass first appeared as a small papule which increased slowly, with a well defined border and a crusted surface. It was painless and slightly pruritic with a tendency to confluence and with oozing on the slightest pressure, when the superficial crust pulled off blood appeared freely and a peculiar penetrating odor was given off. The development of the wartlike nodules was greater from the arm to the distal extremity, giving this limb an elephantiasis-like appearance.

The patient had no general symptoms with the development of these warty nodules and said he had received no previous treatment.

*Family History*—The family history was essentially noncontributory.

*Past Clinical History*—The patient had suffered from malaria and intestinal parasites.

*Physical Examination and General Diagnosis*—The patient was 154 cm in height, 60 Kg in weight, white and pale and resting quietly in bed. Besides

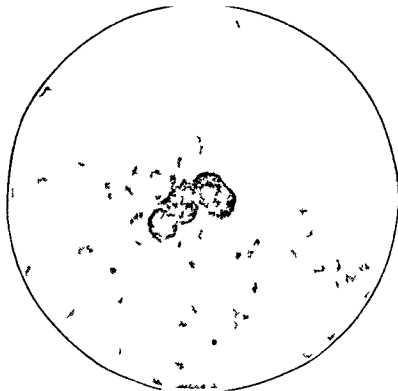


Fig 4 (case 2)—A cluster of sclerotic cells from the crust with a thick wall, one presenting a central septum,  $\times 430$

the wartlike lesions and the elephantiasis-like appearance of the arm, he presented (a) bilateral otosclerosis, general arteriosclerosis and moderate arterial hypertension (160 systolic and 98 diastolic), (b) dental caries, alveolar pyorrhea and lymphoid granulations in the pharynx, (c) moderate anemia of the skin and of the palpebral conjunctiva with thickening and brown color of the orbital conjunctiva, especially at the inner canthus, and (d) hands deformed by chronic osteoarthritis.

*Laboratory Data*—The results of laboratory examinations were as follows: (a) Intestinal parasites (eggs of *Uncinaria*) were present. (b) Anemia of the hypochromic microcytic type was reported. (c) Arthritic changes in the articulation of the wrists and hands were shown by roentgen rays, but there was no change in the bones of hands and forearms. (d) The mycotic nature of the wartlike formations, in which were found abundant sclerotic cells (fig 4) with the accepted characteristics was observed when the crusts were removed and examined microscopically, after being treated with 20 per cent solution of potassium hydroxide.

## HISTOPATHOLOGY

Microscopic examination showed the nodules removed from both patients to be covered with a thick layer of keratinized tissue which on cutting disclosed not only a thickened epidermis with a yellow, soft, gangrenous material in small quantities between the papillary folds but also an equally thickened corium

Microscopic examination confirmed the intense keratinization of the epidermis, some sclerotic cells were encountered, isolated or in groups, brown, with double contour, rounded or polyhedral, and frequently with an intracellular septum and outlined divisions. No degeneration of the cells in the folds of the epidermis was observed, although there was decided thickening of the papillary pegs with extension into the dermis. In general, in both patients the basal layer of the epidermis was well defined. The dermis likewise was thickened and presented many areas of infiltration with round cells and polymorphonuclear leukocytes and some areas of necrosis with characteristic sclerotic cells and hyphae projections. Immediately below the epidermis in case 1 there were a few giant cells within which could be seen the same type of mycotic cells with the accepted characteristics, in case 2 many giant cells were seen, frequently with sclerotic cells inside, which established the microscopic distinction between the two cases already described

## MYCOLOGY

Case 1 (L. C.)—On culture in a Petri dish the fungus previously isolated in test tubes was found equally in Sabouraud's medium (4 per cent) and in corn meal agar at room temperature (25 C) and was present almost within the first seventy-two hours, in a week and a half the culture in each dish was 2 cm in diameter, in five weeks 6 cm (fig 5 A). The culture in general was dark gray, with the central part more elevated than the periphery, covered by fine hairlike projections of olive color that gave it a velvety appearance, with furrows perfectly visible from the center to the periphery and apparently penetrated by the pigment of the fungus. When the culture was ten weeks old the medium was more penetrated by the pigment than before, it was possible to see how the fungus was growing down to the bottom of the medium opposite the superficial layer of slant tubes, and when the projections aforementioned were removed the superficial layer of the medium was black.

The microscopic study of the three week old fungus growing on slides in Czapek's medium at room temperature showed well developed filaments of olive color, 1.5 to 3 microns in diameter and septated every 10 to 30 microns. The filaments were thick walled, dark, described a rectilinear, undulating or spiral course and generally had granular cytoplasm and refractile drops, spherical or oval and of great difference in size (fig 5 B).

Frequently in one week old cultures growing on slides in Sabouraud's medium at room temperature the segmentation of the hyphae was closer than normal, with the thickening of the segment and its wall giving the impression of round regular or irregular articles like the beads of a rosary, from which there frequently grew conidiophores. They were mixed with other hyphae without

close segmentation in which it was possible to see just rounded thickening of the segment with refractile drops and granular cytoplasm giving the impression of chlamydospores. Hyphae were also observed in which the thickening was at one pole of the segment, like a racket, and some showed many segments with lateral prominence of rounded forms more or less pronounced, with a thin wall,

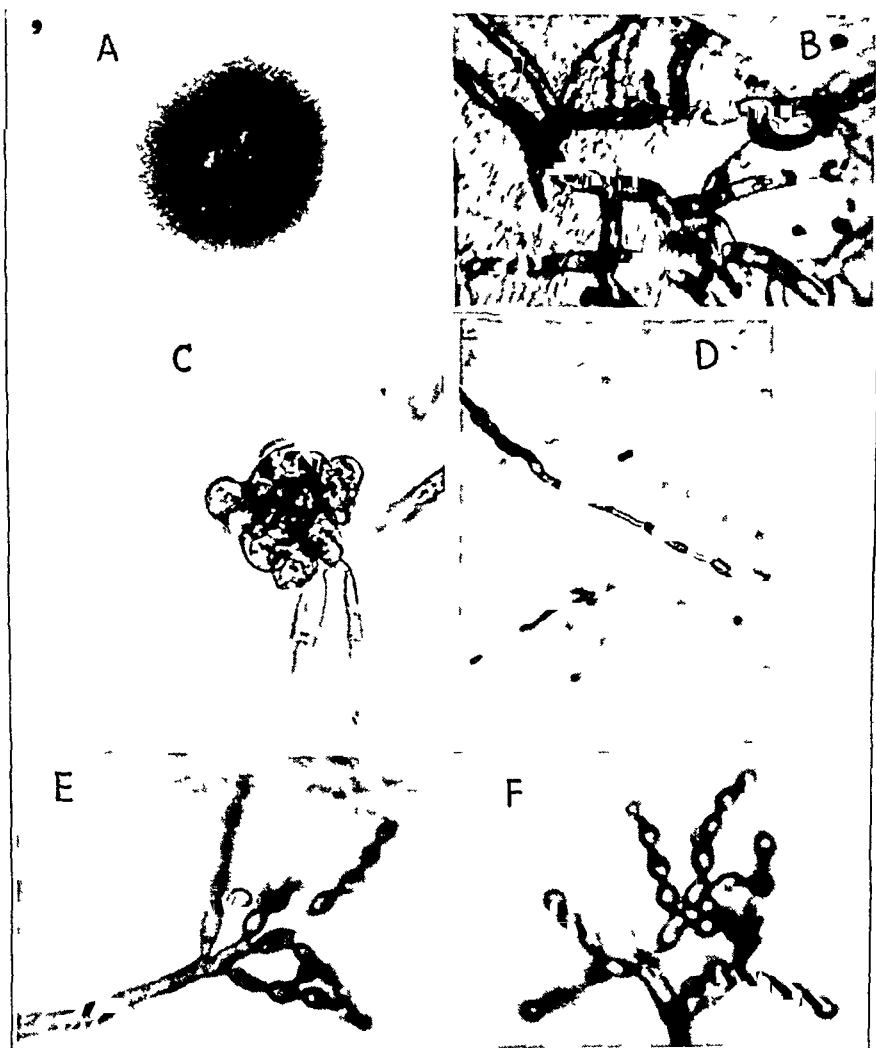


Fig 5 (case 1)—*A*, culture three weeks old, with the central part more elevated than the periphery, dark gray and with hairlike projections perfectly visible at the periphery, *B*, well developed hyphae, with thick wall, dark septated and with refractile drops in the cytoplasm,  $\times 800$ , *C*, culture three weeks old in Sabouraud's medium showing cluster of sclerotic cells,  $\times 1960$ , *D*, thin intercalated segments with hyaline, nongranular cytoplasm with pale and thin wall,  $\times 800$ , *E* and *F*, well developed Hormodendrum's head with large, multiseptated conidiophores, culture two weeks old in Sabouraud's medium,  $\times 1960$

granular protoplasm and refractile drops from which (as from the other irregular segments aforementioned) there frequently grew conidiophores. The evolution of these forms led frequently to the formation of what are called sclerotic cells,

which could be seen well in cultures of three weeks' incubation (fig 5 C) Scattered in the periphery of some slide cultures in Czapek's medium as well as in Sabouraud's medium at room temperature I saw filaments thinner than the normal ones, terminal or intercalated, with hyaline nongranular cytoplasm and pale, thin walls which gave me the impression of nonfertile filaments (fig 5 D)

The commonest form of germination was the *Cladosporioides* type The conidiophores came from the fertile filaments, they were single or multiseptated, with or without granular cytoplasm and refractile drops and generally with hyperpigmentation in the distal portion, from which the conidia arose On occasion the conidia were also spread directly from the hyphae, individually or forming branches of spores In the development of the conidia it was evident that each was smaller than the one from which it was derived (the hyphae from 25 to 35 microns by 7 to 9 microns, the conidia from 15 to 3 microns by 3 to 5 microns), although preserving the same color and form, always oval and with a thick wall Following the development and growth of the conidia, it was possible to predict the formation of a new conidium by the presence of a small hump in the distal portion of the old one with persistence of small germinative buds, on more than one occasion I saw three or more budlike clusters spreading from the same level of the distal extremity of the progenitor This characteristic distinguished it from the *Acrotheca* type of sporulation (fig 5 E and F)

Occasionally in Sabouraud's 4 per cent medium at room temperature I could see conidiophores of the flask-shaped structure, consisting of a single cell distended toward its proximal portion, with distal constriction which opened into a cuplike receptacle, in none of the conidiophores could I see more than one conidium budding out from the constricted portion into its adjacent cup Other flask-shaped structures were found in close association with the *Cladosporioides* type of sporulation, coming out from the same hyphal element and combining the two types of sporulation

I saw definite examples of the third type of sporulation, called *Acrotheca*, in which the conidia were produced acropleurogenously from the conidiophore with shape and size like the ones previously described in the *Hormodendrum*'s head In a culture one and a half weeks old in Sabouraud's medium at room temperature I saw some forms of the pseudoacrotheca type and observed that some heads of *Acrotheca* developed chains of the *Cladosporioides* type, but all these forms were rare, as was the second type previously described

The predominance of the *cladosporioides* type of germination led me to conclude that the fungus of this patient belonged to the genus *Fonsecaea*, namely *F. Pedrosoi*,<sup>61</sup> *Negrom*,<sup>62</sup> variety *Cladosporioides*, Carrion<sup>61</sup>

Case 2 (J R N)—The growth of the fungus in Sabouraud's medium at room temperature in a Petri dish was visible within sixty hours, although its color was a little clearer than that of the previous culture (case 1), it had less power of extension (fig 6 4) and growth, was more elevated in the center than at the periphery and had a hairlike appearance When the growth was removed from the culture medium it was noted that the medium had taken on a black appearance In the three week old medium there was noted a decided tendency of the fungus to present itself as abundant aerial hyphae that arose from the culture and gave it a cotton-like appearance

The microscopic study of the fungus in Sabouraud's medium (4 per cent) at room temperature showed segmented filaments with thick walls, granular cytoplasm and refractile droplets, some had rounded segments like chlamydospores, and



others had thickened segments toward one pole—like a racket—both terminal or intercalated, from which germinative branches generally emerged. Sclerotic cells observed (fig 5 C) in three week old cultures were intercalated or terminal, brown, varying from 7 to 15 microns in diameter, with an intracellular septum and a thick wall

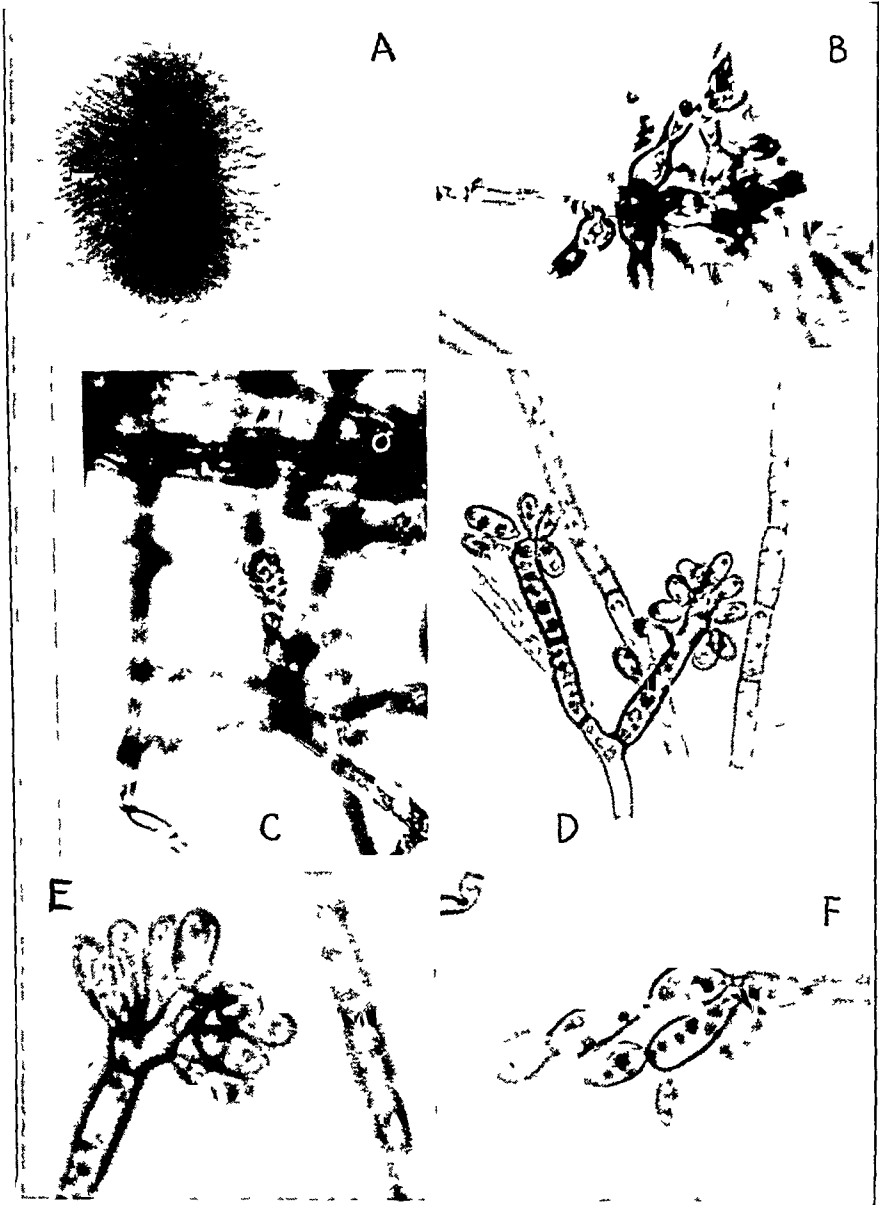


Fig 6 (case 2)—A, culture six weeks old, with the central part more elevated than the periphery and with hairlike projections more visible than in the strain of case 1, B, conidiophores of the flask-shaped structure, emerging directly from the hypha,  $\times 1960$ , C, conidiophore of the same flask-shaped type with a large amount of agglutinated conidia extending from the cup, D and E, conidiophores of the terminal type and germination of the acropleurogenous form characteristic of the *Acrotheca* type,  $\times 980$  and  $\times 1960$  respectively, F, conidiophore of the *Caldosporioides* type of germination,  $\times 1960$

One of the two commonest forms of germination of this second strain was the Phialophora type. The conidiophores were in a flask-shaped structure and emerged from the hypha-like terminal elements or were united to it by a single segment (fig 6 B and C). They were 6 to 10 microns long by 2 to 3 microns wide and opened into a cuplike receptacle, in which they deposited the conidia, generally in a large amount. The conidia were agglutinated temporarily to each other, by a mucilaginous substance secreted by the conidiophore at the moment of sporulation. They were always small, from 1.5 to 2 microns by 2 to 3 microns, with protoplasm finely granulated, pale green and covered with a thin smooth hyaline membrane. They grew separately and in successive form from the neck of the conidiophore. I also observed conidiophores of the branching type and other conidiophores whose basal portion was formed by the same segment of the mycelium.

The other common type of germination was the acropleurogenous form characteristic of the Acrotheca type, in which the conidiophores were generally of the terminal type, and the conidia emerged laterally from the fertile branches (fig 6 D and E) and disposed themselves in a parallel arrangement, which, on separation, showed the small nodular prominence of its implantation. Their size and shape reminded me of what I said of the conidia of the Hormodendrum's head.

Besides these two types of germination I saw a few characteristic forms of the Cladosporioides type, the conidiophores and conidia were similar in form and size to the same germinative type in the first strain previously described (fig 6 F).

The association and relation in quantity between these three types of sporulation led me to classify the fungus of my second patient as the genus *Fonsecaea*, namely, *F. Pedrosoi*,<sup>6a</sup> *Negroni*,<sup>6c</sup> variety *communis* Carrión.<sup>61</sup>

#### TREATMENT

CASE 1 (L. N.) —The patient was treated exclusively with roentgen rays. From Dec 22, 1944 to Jan 6, 1945 he received his first series of radiations with a total of 1,200 r filtered through 2 mm of copper and 1 mm of aluminum. The application was limited in order to observe its reaction. As he did well from January 12 to 17, he received a series of radiations over the whole extension of the nodules with a total of 500 r. From January 30 to February 9 he received a second series of radiations over all the lesions, with a total of 5,000 r. The lesions improved (as demonstrated by the flattening and disappearance of the scabs and the healing of the surrounding skin) with the exception of those nodules situated near the achilles tendon, which presented the same appearance because they had not been irradiated. I then made a scraping of these masses, disclosing abundant sclerotic cells from which were given off filaments that in portions presented thickening like chlamydospores. Acting on this observation, a third and last series of irradiations was begun the next day. They were given over all the lesions, from March 23 to April 4, with a total of 5,000 r. The patient was discharged from the hospital, and so my opportunity to observe any change in his condition ceased.

CASE 2 (J. R. N.) —Surgical removal of the warty nodules was prescribed. After the excision of the warty masses by electrocautery, the whole surface was electrocoagulated especially on the border. The healing was slow, and when complete

repeated scraping did not show sclerotic cells. Nevertheless, for prophylactic purposes the patient received a series of ten irradiations with a total of 1,000 r. I have no doubt of the success of the surgical treatment in this case.

#### SUMMARY

Two new cases of chromoblastomycosis are reported in this paper, both in white farmers from the Republic of Panama, aged 48 and 49 years respectively. The first patient had lesions of eight and a half years' duration, which extended from the knee to the right sole. The second patient had lesions of two and a half years' duration, and these were localized from the middle third of the left forearm to the hand of the same side.

The study of the fungus in the first patient (in a 4 per cent solution of Sabouraud's medium as well as in Czapek's medium, at room temperature) showed abundant forms of the *Cladosporioides* type, with very few characteristic forms of the *Phialophora* and *Acrotheca* types. The fungus of the second patient showed a large amount of forms of the *Phialophora* and *Acrotheca* types and very few forms of the *Cladosporioides* type. The flasks of the strain of the first patient did not show more than one conidium in each receptacle, and the *Acrotheca* forms never had more than three pairs of conidia, while the similar forms of the fungus of the second patient presented flasks with abundant agglutinated conidia and *Acrotheca* forms with more than three pairs of conidia. In cultures of both fungi there were found cells with the same character as the sclerotic cells aforementioned.

The treatment was different in each of these cases and was in accordance with the extent of the lesion and the time of evolution. The first patient received only roengen ray treatment, with a total of 11,700 r given in series from Dec 22, 1944 to April 4, 1945 and with periods of rest between. The second patient was treated surgically and the extirpation of the nodules was followed by electrocoagulation, when healing was established a series of irradiations was given, with a total of 1,000 r, from March 23 to April 4.

Examination of the first patient a few days before his departure from the hospital and before the completion of the last series of irradiations showed that he had improved, but the nodular masses had persisted although they were smaller than on his admission. I wish to stress the fact that the warty mass over the achilles tendon, which had not been irradiated, still showed abundant sclerotic cells with filaments and rounded bodies like chlamydospores, ten days before his departure from the hospital, this was irradiated with a total of 5,000 r. Although it was not possible for me to control the disease of the patient before he left the hospital I believe that the patient had improved but I am not certain of the total cure of his mycotic disease.

The recent examination of the second patient was most promising. Repeated scraping of the periphery of the scars before they were irradiated did not show the characteristic sclerotic cells, therefore, 'I feel sure that the patient was cured and that the cure should be attributed to the surgical treatment (electrocautery)

Dr J M Nuñez, Chief of the Medical Service of the Santo Tomas Hospital, Dr H C Clark, Director of the Gorgas Memorial Laboratory, Lieut H Trapido, from the same laboratory, and Dr E S Wedding, from the Gorgas Board of Health, made suggestions and assisted in this work

## RAT MITE DERMATITIS

Acariasis Caused by the Tropical Rat Mite, *Liponyssus Bacoti* Hirst

M E LOWELL, M D

WESTFIELD, N J

IT IS possible that rat mite dermatitis due to *Liponyssus Bacoti* Hirst is more frequent than the literature indicates. Bishopp,<sup>1</sup> Shelmire and Dove<sup>2</sup> in Texas, Weber<sup>3</sup> in Chicago and C R Anderson<sup>4</sup> in Los Angeles have reported cases. Because this mite may be the vector of endemic typhus and can become an occupational hazard, recognition of the dermatitis and the mite are important. No report has been made of its occurrence in this part of the United States.

### REPORT OF CASES

A woman employed in an electrical industry noticed some small red marks on her arms, neck, abdomen and legs, associated with pruritus. She discontinued work for one week, and the rash and symptoms disappeared. There was an immediate recurrence of the process as soon as she resumed her occupation. Four other employees were similarly affected at the time.

An examination of the working environment revealed the presence of many minute, light gray, rapidly crawling mites in the paper tissue used for wrapping. Further investigation showed that a campaign of rat extermination by means of poisonous bait had been instituted and that several dead brown rats had been seen by the employees. These employees worked on one of the upper floors in a steel and concrete building.

The cutaneous lesions consisted of  $\frac{1}{4}$  inch (0.6 cm) erythematous macules, which, for the most part, were scattered over the arms and shoulders, although a few lesions were present on the neck, abdomen and legs. In some lesions there was a small central punctum. In a few of the older lesions the central mark was still visible, surrounded by a light pigmentation. Neither grouping of the lesions nor arrangement in linear distribution could be noted. There was no predilection for the anterior or posterior surfaces. At the spot where the patient had been bitten pruritus was mild. Itching seemed to be caused by the crawling of the mites on the skin rather than by their bites. Neither the woman nor the

1 Bishopp, F C. The Rat Mite Attacking Man, Circular 294, United States Department of Agriculture, Bureau of Entomology, 1923, pp 1-4.

2 Shelmire, B, and Dove, W E. The Tropical Rat Mite, *Liponyssus Bacoti* Hirst, 1914, the Cause of a Skin Eruption of Man, and a Possible Vector of Endemic Typhus Fever, J A M A **96** 579-584 (Feb 21) 1931.

3 Weber, L F. Rat Mite Dermatitis, J A M A **114** 1442 (April 13) 1940.

4 Anderson, C R. Rat Mite Dermatitis, Arch Dermat & Syph **50** 90-95 (Aug) 1944.

other employees had an elevation of temperature, and all were found to be in good health. After the infested paper had been removed and the floor sprayed with insecticide, no new lesions developed.

#### COMMENT

The mites are oval, light gray and actively motile. They vary in length from 0.5 to 0.75 mm. Some were found to contain blood. It has been stated that the mites prefer warmth, but this could not be verified.



Rat mite (*Liponyssus bacoti* Hirst),  $\times 165$

in the case reported, nor could it be verified by placing the mites in a long test tube, half of which was kept warm. Under these conditions the mites showed no inclination to favor the warmer end. They were easily destroyed by heat, as when the test tube was placed under hot tap water (150°F) for a few minutes. The mites have four pairs of legs attached to the ventral surface of the fused cephalothorax and are further character-

ized by pointed chelae of the mandibles. The medial hypostome projects in a needle-like fashion. The mites require four blood meals to complete their life cycle. The rickettsial organism of endemic typhus, if present, is passed from one generation to the next through the eggs. A female mite can live about ten days without feeding. Eggs require from four to six days to hatch, and such mites can then live for twelve days without feeding. It has been estimated that eighteen days must elapse after a place has been cleared of rats before all mites are dead, unless some insecticide spray is used.

#### SUMMARY

An eruption was determined to be due to *Liponyssus bacoti* Hirst. No cases of the disease have been reported in the New York metropolitan area. This dermatitis can become an industrial hazard. During any campaign for the extermination of rats, preventive measures should be taken by thorough house cleaning and by using an insecticide spray. The rat mite can serve as a vector of endemic typhus. In cases of disease suspected to be due to insect bites, rat mite dermatitis should be kept in mind.

## URINARY EXCRETION OF PORPHYRIN IN DERMATOSES

LIEUTENANT I ZELIGMAN (MC), USNR

**I**NTEREST in the physiologic and pathologic significance of the porphyrins has increased considerably during the last two decades, mainly as a result of the thorough chemical investigations of Hans Fischer<sup>1</sup> and his collaborators. Whereas the rare metabolic anomalies characterized by enormously raised excretion of porphyrins which were studied in the pioneer work of Garrod<sup>2</sup> and Gunther<sup>3</sup> were originally medical curiosities, the more precise methods developed during the last fifteen years have shown that the porphyrins play a vital part in both normal and pathologic pigment metabolism.

Anderson<sup>4</sup> was the first to suggest the association of porphyrins with abnormal sensitivity to light. In 1898 he described two brothers suffering from recurrent bullous lesions of the uncovered parts of the body, which he diagnosed as *hydroa estivale*. The urine of both took on a burgundy red color at times, and chemical examination revealed the presence of a pigment with spectral absorption bands coinciding with those of hematoporphyrin, a substance known to be derivable from hemoglobin or hemin. Hematoporphyrin is now known not to appear in either normal or pathologic urines, but there are other porphyrins with similar absorption spectrums which may have been present. Porphyrin was soon demonstrated in the urine in a number of cases of this type and Gunther's<sup>5</sup> summaries show a certain degree of correlation between urinary excretion of porphyrin and *hydroa*. McFarland and Strain<sup>6</sup> and Brunsting, Brugsch and O'Leary<sup>7</sup> have studied excretion of porphyrin in the urine in various cutaneous diseases.

From the Departments of Dermatology and Biochemistry, Columbia University College of Physicians and Surgeons, and from the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University

1 Fischer, H., and Orth, H. *Die Chemie des Pyrrols*, Leipzig, Akademische Verlagsgesellschaft, 1937

2 Garrod, A. E. *On Hematoporphyrin as a Urinary Pigment in Disease*, *J. Path. & Bact.* **1**: 187-197, 1892

3 Gunther, H. *Die Hamatoporphyrie*, *Deutsches Arch. f. klin. Med.* **105**: 89-146, 1911

4 Anderson, T. M. *Hydroa Estivale in Two Brothers, Complicated with the Presence of Hematoporphyrin in the Urine*, *Brit. J. Dermat.* **10**: 1-4, 1898

5 Gunther, H. *Die Bedeutung der Hämatoporphyrine in Physiologie und Pathologie*, *Ergebn. d. allg. Path. u. path. Anat.* **20**: 608-764, 1922, footnote 3

6 McFarland, A. R., and Strain, W. H. *Significance of Porphyrin Content of Urine in Dermatoses Associated with Sensitivity to Light*, *Arch. Dermat. & Syph.* **38**: 727-736 (Nov.) 1938

(Footnotes continued on next page)



More recent studies of the chemical and physical properties of the porphyrins, their distribution in nature and their metabolic functions have shown the whole field to be extremely complicated. The work of Fischer and others on their chemical constitution has done much to clarify the confusion resulting from earlier clinical observations, which disregarded the important differences in structure, source and function among the different porphyrins. Space does not permit a discussion of the voluminous work in this field, and the reader is referred to the monographs of Carrie,<sup>8</sup> Vannotti<sup>9</sup> and Dobriner and Rhoads<sup>10</sup>. Some of the salient points follow. The various porphyrins, such as uroporphyrin, coproporphyrin and hematoporphyrin, can each occur in four isomeric forms which differ in the position of the substituents in the pyrrole groups. These have been designated by Fischer as porphyrins of the I, II, III and IV series. The protoporphyrin which forms the nucleus of hemoglobin belongs to series III, whereas the coproporphyrin normally excreted in the urine and feces belongs to series I. Since conversions from one to the other series are apparently impossible in the body, the coproporphyrin commonly found cannot be considered a direct derivative or end product of hemoglobin metabolism. Its origin is obscure. One hypothesis is that it is derived directly from food. Some evidence as to this will be presented in this paper. Dobriner and Rhoads<sup>10</sup> found a striking increase in the urine during regeneration of blood and suggested that it might be a functionless by-product of the synthesis of hemoglobin. Urinary excretion of coproporphyrin I is increased after various forms of hepatic damage and in any fever.

In congenital porphyria, uroporphyrin as well as greatly increased amounts of coproporphyrin appears in the urine. Uroporphyrin and coproporphyrin of series III and also of series I have been recovered. In many of these cases lesions of hydroa estivale develop. In some (approximately one third) of the reported cases of hydroa estivale, porphyrins appear in the urine in grossly demonstrable amounts. Again, uroporphyrin and coproporphyrin of both series I and series III have been reported.

The experiments of Meyer-Betz<sup>11</sup> show that the injection of hematoporphyrin III can produce intense sensitization to light. This porphyrin

7 Brunsting, L. A., Brugsch, J. T., and O'Leary, P. A. Quantitative Investigation of Porphyrin Metabolism in Diseases of Skin, *Arch Dermat & Syph* **39** 294-307 (Feb.) 1939.

8 Carrie, C. *Die Porphyrine, ihr Nachweis, ihre Physiologie und Klinik*. Leipzig, Georg Thieme, 1936.

9 Vannotti, A. *Porphyrie und Porphyrinkrankheiten*, Berlin, Julius Springer, 1937.

10 Dobriner, K., and Rhoads, C. P. The Porphyrins in Health and Disease, *Physiol Rev* **20** 416-468, 1940.

has never been found in the body or excreta, though it is easily produced from hemoglobin in vitro. Evidence as to the photosensitizing power of the other porphyrins is conflicting, depending somewhat on the test object and the wavelength of the light employed. Most observers agree that the sensitizing power decreases in the following order: hematoporphyrin, uroporphyrin, coproporphyrin and protoporphyrin. Clinically, the appearance of uroporphyrin seems the most significant. However, not all patients with *hydra estivale* excrete uroporphyrin, and not all patients excreting uroporphyrin are clinically sensitive. Hence, while there is much to suggest that hypersensitivity to light may be produced by the accumulation of porphyrins in the body, the evidence is not clear, especially as it concerns coproporphyrin I.

The methods used for the clinical study of porphyrin excretion may be divided into three groups:

1. Those depending on colorimetric measurement of various concentrations of the urine. These all have the defects that they are not sufficiently sensitive to demonstrate porphyrins present in normal urine and are interfered with by other urinary pigments.

2. Those methods depending on the measurement of the intensity of fluorescence of porphyrin. Such measurements have been undertaken by a variety of methods, many of which are sensitive and accurate but require complicated apparatus.

3. The method depending on the comparison of absorption band detectability at various dilutions. It is the method used in this work. It is based on that of Lageder<sup>12</sup> and was chosen because it permitted fairly sensitive determinations with relatively simple apparatus. This method of absorption band detectability has been employed by Kapp and Coburn<sup>13</sup> and by Maechling<sup>14</sup>.

#### QUANTITATIVE METHOD USED

The method of extraction of coproporphyrin used here was a modification of that of Dobriner and Rhoads<sup>15</sup>. The total volume of the twenty-four hour specimen of urine was measured. To 250 cc of the specimen, 3 cc of saturated

11. Meyer-Betz, F. Untersuchungen über die biologische Wirkung des Hämoporphyrins und anderer Derivate des Blut- und Gallenfarbstoffes, *Deutsches Arch f klin Med* **112** 476-503, 1913.

12. Lageder, K. Klinische Porphyrinuntersuchungen mit einer quantitativen spektroskopischen Methode. *Arch f Verdauungskr* **56**:237-265, 1934.

13. Kapp, E. M., and Coburn, A. F. Studies on the Excretion of Urinary Porphyrin in Rheumatic Fever, *Brit J Exper Path* **17**:255-266, 1936.

14. Maechling, E. H. Urinary Porphyrin Before and After Hydrolysis, *J Lab & Clin Med* **26** 1676-1678, 1941.

15. Dobriner, K., and Rhoads, C. P. Quantitative Determination of Urinary Coproporphyrin, *New England J Med* **219** 1027-1029, 1938.

sodium acetate solution and 75 cc of glacial acetic acid were added. The acidified urine was then extracted twice with an equal volume of ether, and the ethereal solutions were combined. The combined ethereal solution was washed twice with  $\frac{1}{2}$  volume of distilled water containing some sodium acetate (approximately 10 cc of saturated sodium acetate solution to 600 cc of distilled water). The washed ethereal solution was extracted three times with 10 cc of 5 per cent hydrochloric acid and the acid extracts were combined. The combined acid solution was neutralized to congo red with saturated sodium acetate, and 10 cc of glacial acetic acid was added. This was extracted twice with equal volumes of ether and the ethereal solutions combined. The combined ethereal solution was washed twice with dilute sodium acetate solution (approximately 10 cc of saturated sodium acetate solution to 600 cc of distilled water). The washed ethereal solution was extracted three times with 10 cc of 0.5 per cent hydrochloric acid. An equal volume of chloroform was added to the combined acid solution, and the mixture was allowed to separate. The acid solution was neutralized to congo red with saturated sodium acetate solution, and 2 cc of glacial acetic acid was added. This was then extracted twice with 10 cc of ether and the ethereal solutions combined.

It was found that for most normal urines the chloroform step may be omitted. Each specimen was extracted twice, once as previously outlined. Another 250 cc of the urine specimen was first treated with 18 per cent hydrochloric acid solution and left overnight. To this was added sodium hydroxide till it became alkaline to litmus. Then glacial acetic acid was added till the solution was acid, and the first extraction with equal volumes of ether was pursued as previously outlined. The extraction giving the higher reading was recorded. It has been shown by Maechling<sup>14</sup> that this procedure often increases the amount of porphyrin recoverable by the method here used—possibly by the hydrolysis of chromogens (porphyrinogens) or by the splitting of conjugated porphyrins.

Quantitative estimation of the amount of coproporphyrin contained in the final acetic acid-ether extract was based on Lageder's<sup>12</sup> method, as employed by Kapp and Coburn<sup>13</sup> and by Maechling<sup>14</sup>. The spectroscopic examination was made with a Bausch and Lomb wavelength spectrometer no 628. The source of light was a Burn Base Down Projection bulb—Mazda General Electric, 6 volts, 18 amperes. Hematoporphyrin, which spectroscopically is almost if not absolutely identical with coproporphyrin, was employed as a standard. By the use of the comparison prism of the Bausch and Lomb wavelength spectrometer, when the spectrums from two light sources of hematoporphyrin and coproporphyrin were superimposed, the bands were identical both in ether and in a solution of hydrochloric acid. This confirmed the observations of Watson.<sup>16</sup>

A series of standard hematoporphyrin solutions in ether were prepared and the limits of their absorption bands recorded. When 14 micrograms of hematoporphyrin in 16 cc of ether solution was contained in a 200 mm polariscope tube, a relatively faint band at 6,230 angstrom units was visible. Similarly, when 3 micrograms of hematoporphyrin in 16 cc of ether solution was contained in a 200 mm polariscope tube an absorption band at 6,230 angstrom units was barely visible. These end points of absorption band visibility were used for measuring the ethereal solutions of coproporphyrin. All test solutions were brought to

16 Watson, C. J. *The Porphyrins and Their Relation to Disease*, in Christian, H. A. *Oxford Medicine*, New York, Oxford University Press, 1938, vol 4, p 8.

these end points by dilution or by decreasing the length of the solution-containing cells

Waldenstrom's<sup>17</sup> chromatographic analysis was used for isolation of uroporphyrin. After removal of the ether-soluble porphyrin, the acetic acid-soluble aqueous portion was passed through an adsorption column of Merck's aluminum oxide and eluted with 12 per cent ammonia. The ammoniac solution would be expected to show the alkaline spectrum of uroporphyrin were the latter present. Uroporphyrin was not found in the urines examined.

The acetic acid-ether spectrum of either coproporphyrin or hematoporphyrin was found to be

I	6,250 6,200 Å
II	5,970 Å
III	5,810—5,690 5,660 Å
IV	5,320 5,240 Å
V	5,050 1,980 4,930 4,880 1,830 Å

#### DIURNAL VARIATIONS OF URINARY PORPHYRIN EXCRETION

An attempt was made to learn the daily variations of urinary excretions of porphyrin and to study such excretions on varying dietary regimens. A 26 year old white man weighing 72 Kg was studied for three weeks. He was given the following diets for three weeks: first week, meat once daily; second week, meat twice daily; and third week, no meat. Twenty-one specimens were studied, and, despite the reports of increased porphyrinuria accompanying the intake of meat by Kammerer and Gursching,<sup>18</sup> Franke and Fikentscher,<sup>19</sup> Vannotti<sup>9</sup> and others, no increased excretion was noted with the meat diet. The daily excretion of urinary coproporphyrin with a diet containing meat once daily varied from 64.9 to 207.9 micrograms, with an average of 105.4 micrograms for the 7 specimens. That with a diet containing meat twice daily varied from 83.2 to 112.1 micrograms, with an average of 94.6 micrograms for the 7 specimens. The daily excretion of urinary coproporphyrin with a meatless diet was 44.2 to 190.9 micrograms, with an average of 118 micrograms for the 7 specimens.

Another series of quantitative determinations on the same subject was performed several months later. He was given a meat regimen for one week, a meat-free regimen for the second week and a varying diet (sometimes including meat) the third week. Again there were decided daily variations, and again there were no significant differences with the different diets. The general average of excretion was somewhat lower than that during the previous investigation. Here the coproporphyrin excreted in twenty-four hours with a meat diet varied from 52.2 to 101.6 micrograms, with an average excretion of 75.4 micrograms for the 7 specimens. The excretion with a meatless diet varied from 72.6 to 105.4 micrograms, with an average of 89.4 micrograms for the 7 specimens. The

17 Waldenstrom, J. Untersuchungen über Harnfarbstoffe, hauptsächlich Porphyrine mittels der chromatographischen Analyse, *Deutsches Arch f klin Med* **178** 38-49, 1935.

18 Kämmerer, H., and Gursching, J. Vergleichende Untersuchungen über den Porphyringehalt tischfertiger Nahrungsmittel als der möglichen Quelle der Körperporphyrine, *Verhandl d deutsch Gesellsch f inn Med* **41** 486-494, 1929.

19 Franke, K., and Fikentscher, R. Die Bedeutung der quantitativen Porphyrinbestimmung mit der Lumineszenzmessung für die Prüfung der Leberfunktion und für Ernährungsfragen, *München med Wchnschr* **82** 171-172, 1935.

average of specimens excreted with a varying diet was 81.5 micrograms per twenty-four hours for 6 specimens

An unusually large amount of chlorophyll ingested one day resulted in the excretion of 106.7 micrograms of porphyrin. A meatless diet, but with the ingestion of a considerable amount of blood, was accompanied with the excretion of only 54.2 micrograms. Here again there were striking daily variations, and yet there seemed to be definite limitations. Again, ingestion of meat was not accompanied by an increase of porphyrinuria.

#### NORMAL URINES

Twenty twenty-four hour specimens of urine from 15 normal adults, aged 20 to 31, were studied for quantitative coproporphyrin excretion. The total twenty-four hour coproporphyrin excretion in the urine varied from 50.9 to 192.7 micrograms, with an average of 123.7 micrograms for the 12 specimens from males and of 107.9 micrograms for the 8 specimens from females. The average for all 20 specimens was 117.4 micrograms.

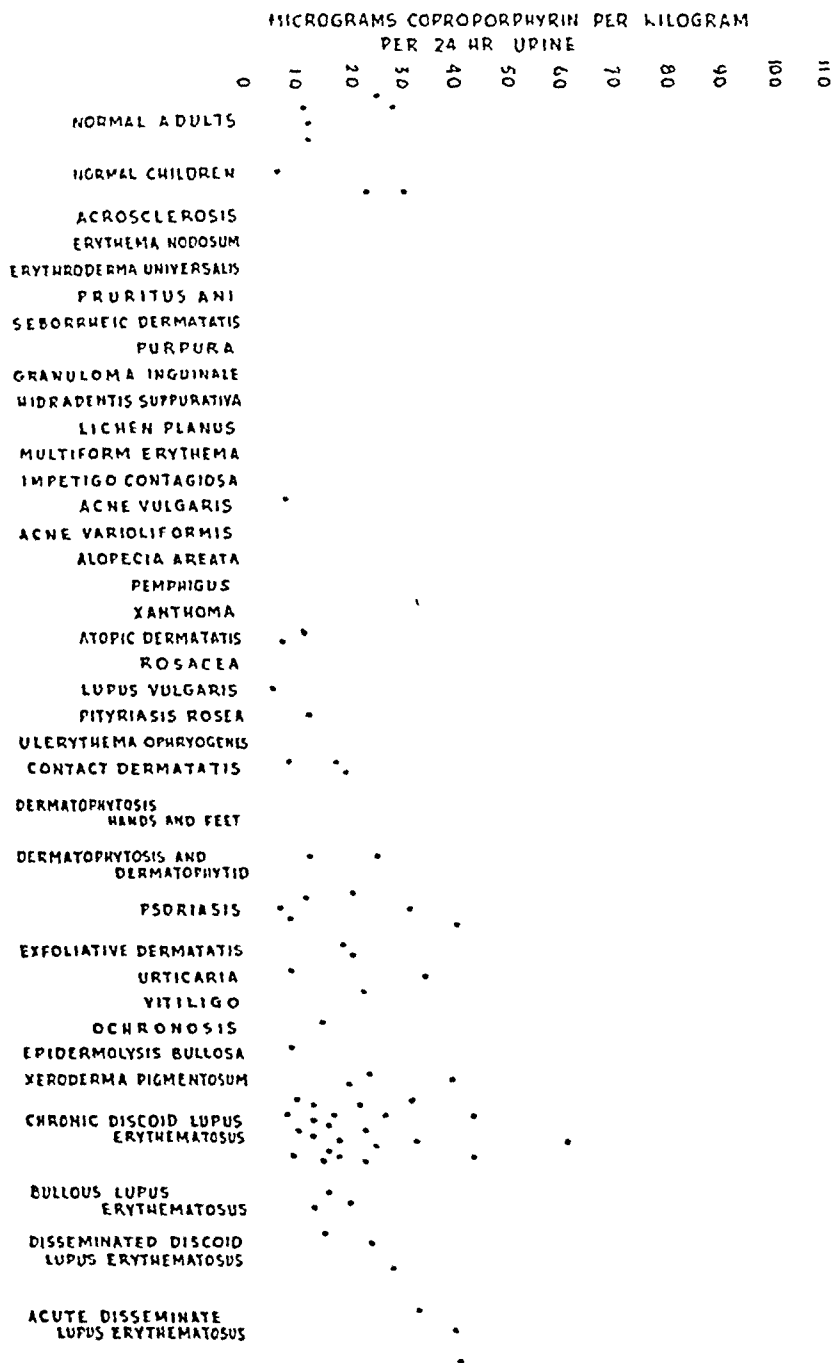
The urinary coproporphyrin excretion per kilogram of body weight varied from 0.9 to 3 micrograms per twenty-four hour specimen and averaged 1.9 for the 12 specimens from males and 1.9 for the 8 specimens from females. It averaged 1.9 micrograms per twenty-four hour specimen per kilogram for all 20 specimens.

Though few data on the subject are available, some writers have stated that the urinary coproporphyrin of normal children is less than that of normal adults. Eighteen children living in an orphanage, ranging in age from 7 to 14 years, were studied for urinary coproporphyrin excretion. The minimum twenty-four hour urinary coproporphyrin excretions were 15.1 and 17.2 micrograms, while the two highest excretions were 117.1 and 113.1 micrograms. The average excretion was 71.2 micrograms. The average total twenty-four hour coproporphyrin excretion of these children was definitely less than that of the adults studied.

Urinary excretion of coproporphyrin of the children in terms of body weight varied from 0.6 to 3 micrograms per twenty-four hours per kilogram and averaged 2.1 micrograms per twenty-four hours per kilogram of body weight. This compares with 1.9 micrograms per twenty-four hours per kilogram of body weight in adults, approximately the same.

A few patients with anemia were studied for coproporphyrinuria. A Negro man, aged 25, who had sickle cell anemia and whose urine gave a positive reaction to Ehrlich's paradimethylaminobenzaldehyde reagent, excreted 168 micrograms of coproporphyrin in twenty-four hours. A white girl, aged 3 years, with microcytic anemia excreted 74.3 micrograms of coproporphyrin, and another 3 year old child, with erythroblastic anemia, had 99.6 micrograms. These excretions in children were

definitely higher than their body weights warranted. Two white women, aged 59 and 38, with microcytic anemia excreted 120.9 and 77.4 micrograms of coproporphyrin per twenty-four hours, respectively. These



Excretion of coproporphyrin in urine during twenty-four hours by normal persons and by patients with various dermatoses

values were certainly within normal limits. A white woman, aged 42, with Hodgkin's disease of the skin, aplastic anemia, hepatomegaly and splenomegaly had a urinary coproporphyrin level of 252.7 micro-

grams, her urine gave a positive reaction to Ehrlich's reagent. This high excretion might have been associated with hepatic insufficiency.

Three white adults, aged 45, 60 and 69, with obstructive jaundice had urinary levels of coproporphyrin of 237.6, 683.5 and 162.6 micrograms, respectively. A white woman, aged 35, with toxic hepatitis excreted 717.1 micrograms of coproporphyrin per twenty-four hour specimen of urine. In all 4 of these cases there were positive reactions to Ehrlich's reagent. Three of these results are in accordance with the reports of greatly increased coproporphyrinuria in hepatic diseases.

#### PORPHYRIN EXCRETION IN DERMATOSES

A great deal of work has been done in relating porphyrin metabolism to various dermatologic diseases, but few extensive investigations have been undertaken relative to the excretion of coproporphyrin in urine in the various dermatoses, particularly the photodermatoses. McFarland and Strain<sup>6</sup> found normal urinary porphyrin in sunlight urticaria, sulfanilamide photodermatoses, lupus erythematosus, rosacea, tinea and eczema and increased porphyrinuria in arsenical exfoliative dermatitis. Brunsting, Brugsch and O'Leary<sup>7</sup> reported normal values for urinary porphyrin in cases of ordinary sensitivity to light, pellagra, discoid or disseminate lupus erythematosus, psoriasis, eczema, secondary syphilis, pityriasis rosea, lichen planus and dermatomyositis and increased excretions of porphyrin in cases of sulfanilamide photosensitivity, neorarsphenamine exfoliative dermatitis, erythroderma associated with Hodgkin's disease of the skin, leukemia cutis, erythema induratum and scrofuloderma. In this study, the same methods of extraction and estimation were utilized for outpatients and hospitalized patients with various dermatoses as previously described for the normal persons. One hundred and twenty-six patients were studied. Most of the patients with dermatoses excreted normal amounts of coproporphyrin in the urine. A patient with acrosclerosis resembling the end stage of hydroa estivale was studied and found to have normal porphyrin excretion. One patient with erythema nodosum, 1 with erythroderma universale, 1 with pruritis ani, 2 with seborrheic dermatitis, 2 with purpura, 1 with granuloma inguinale, 1 with hidradenitis suppurativa, 3 with lichen planus, 2 with erythema multiforme, 2 with impetigo contagiosa, 1 with acne varioliformis, 3 with alopecia areata, 2 with pemphigus, 4 with atopic dermatitis, 1 with rosacea, 1 with lupus vulgaris, 5 with pityriasis rosea, 1 with keratosis pilaris (ulerythema ophryogenes), 6 with dermatitis venenata, 4 with dermatophytosis and dermatophytid, 3 with arsenical exfoliative dermatitis and 2 with vitiligo had normal excretion of coproporphyrin. Four with acne vulgaris had normal excretions, but 1 had porphyrin levels above normal, the reason for this could not be determined. The porphyrin excretion of a patient with xanthoma diabeticorum

was within normal limits, but 1 with xanthoma tuberosum multiplex had high levels. Two patients with dermatophytosis of hands and feet, proved mycologically, had normal values, but 1 had a borderline figure of 3 micrograms per kilogram, and 1, a figure of 3.9 micrograms per kilogram. Three patients with urticaria had normal values and 1 with a history of sensitivity to sunlight showed no urticaria or hypersensitivity to ultraviolet irradiation while under observation, there was no opportunity for exposure to other rays. A patient with ochronosis and alkaptonuria had a normal excretion of coproporphyrin and no uroporphyrin, homogentisic acid was isolated from the urine. Two patients with epidermolysis bullosa hereditaria and 1 with hydroa estivale had normal excretions of coproporphyrin and no uroporphyrin. Three with xeroderma pigmentosum had normal values, and 1 had a higher excretion of coproporphyrin than normal.

Of 29 patients with discoid lupus erythematosus, 22 had normal urinary coproporphyrin excretions, and the others excreted 3, 3.5, 3.1, 4.2, 6, 4.2 and 3.7 micrograms of coproporphyrin per kilogram of body weight. Normal values were obtained in 4 patients with erythema multiforme type of lupus erythematosus. One patient with disseminated discoid lupus erythematosus excreted 3.3 micrograms of coproporphyrin per kilogram, but 4 others with the same disease excreted normal amounts. All 4 patients with acute disseminate lupus erythematosus had high levels of coproporphyrin excretion; one would expect to find an increase because of the accompanying low grade hyperpyrexia.

#### COMMENT

The subject of particular interest was whether eruptions commonly considered to be caused or aggravated by sunlight, such as lupus erythematosus, hydroa estivale, xeroderma pigmentosum and solar urticaria, were characterized by an increased coproporphyrinuria or the excretion of uroporphyrin. Uroporphyrin was not found in any instance. In most cases the coproporphyrin excretion was within the normal range, but in some cases of diseases without a relation to light, 1 of acne vulgaris, 1 of xanthoma tuberosum multiplex, 1 of dermatophytosis and 2 of psoriasis, there was a coproporphyrin excretion of 3 or more micrograms per kilogram of body weight. As has been shown in the literature, there are numerous factors causing increased excretion of porphyrin, which may have accounted for these findings.

The differentiation between human and animal ochronosis was well shown by the case studied. Though animal ochronosis is in reality a type of congenital porphyria, this, a typical case of human ochronosis, showed alkaptonuria and homogentisic acid but no uroporphyrin and only normal coproporphyrin values.



Unfortunately, the patient with a history of sensitivity to sunlight and urticaria with increased coproporphyrinuria failed to cooperate sufficiently for a complete study. His response to ultraviolet radiation from a cold quartz mercury vapor lamp was normal, but the hypersensitivity in such cases has been shown to be at wavelengths of 4,100 to 5,300 angstrom units.

Epidermolysis bullosa hereditaria has been reported associated with congenital porphyria. The 2 cases studied showed no uroporphyrin and only normal coproporphyrin levels. A case of hydroa estivale yielded normal values of porphyrin. In only approximately one third of the cases of hydroa estivale in the literature has the disease been associated with abnormal porphyrin excretion.

Three patients with xeroderma pigmentosum had normal values, and 1 had a higher level of excretion. No reason for this difference could be ascertained.

Discoid lupus erythematosus is recognized as being aggravated by exposure to light. Twenty-two of 29 patients had normal excretions of porphyrin, while data for the other 7 showed 3 or more micrograms of coproporphyrin per kilogram of body weight. Thus, a goodly number of these patients had high levels of coproporphyrin excretion. Yet an increased excretion of coproporphyrin cannot be said to be characteristic of patients with discoid lupus erythematosus, since over three fourths of such patients studied had normal values.

Four patients with the erythema multiforme type of lupus erythematosus had normal levels of coproporphyrin excretion.

One of 5 patients with disseminated discoid and subacute disseminated lupus erythematosus had values for urinary coproporphyrin excretion higher than normal, the other 4 had normal values. These varieties of lupus erythematosus are likewise aggravated or provoked by exposure to light.

It was not surprising to find that all 4 patients with acute disseminate lupus erythematosus had increased urinary excretion of coproporphyrin, since all diseases characterized by hyperpyrexia may be accompanied with increased excretion of porphyrin. Therefore one is not justified in associating the sensitivity to sunlight in a case of acute disseminate lupus erythematosus with the increased coproporphyrinuria.

#### SUMMARY

Methods for qualitative and quantitative determinations of porphyrins in the urine are reviewed.

The quantitative method for measuring coproporphyrinuria and the qualitative method for uroporphyrinuria as employed in this investigation are given. The method for estimating coproporphyrinuria is based on a spectroscopic absorption band end point.

There are substantial daily variations of urinary coproporphyrin excretion in normal persons, yet there are evident normal limitations. Increase of coproporphyrinuria was not found to accompany ingestion of meat.

According to the method employed, the normal variations of urinary coproporphyrin excretion in 20 specimens from 15 adults aged 20 to 31 were 50.9 to 192.7 micrograms, with an average of 123.7 micrograms. The urinary coproporphyrin excretion per kilogram of body weight varied from 0.9 to 3 micrograms and averaged 1.9 micrograms.

Of 18 children from 7 to 14 years of age, the urinary coproporphyrin excretion varied from 15.1 to 117.1 micrograms and averaged 71.2 micrograms. In terms of body weight, they excreted from 0.6 to 3 micrograms and an average of 2.1 micrograms in twenty-four hours per kilogram of body weight.

One hundred and twenty-six patients with dermatologic diseases were studied from the standpoint of urinary porphyrin excretion. No uroporphyrin was found in any case. Most of the coproporphyrin levels were within the normal range. A few persons with dermatoses unrelated to sensitivity to light had a high coproporphyrin level in the urine, whereas most of those with photodermatoses had normal values. Though a greater proportion of photodermatoses than of other dermatoses are accompanied with increased coproporphyrin in the urine, such an increase cannot be used as a diagnostic criterion of the photodermatoses.

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## ALLERGIC DERMATOSES COMPLICATING PENICILLIN THERAPY

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**T**OXIC reactions following penicillin therapy in human beings are uncommon. Few significant complications were noted in the several large series of cases<sup>1</sup> reported in the current literature. The reactions to the drug itself are usually of an allergic nature and are then manifested clinically as some type of dermatitis. The manner in which one is exposed to the penicillin, whether externally or parenterally, will determine within limits the nature of the dermatitic response. There are three clinical types of reaction to the commercial penicillin: (1) urticaria, (2) the erythematovesicular group of reactions and (3) contact dermatitis. The first two follow the injection route only, while contact dermatitis occurs only after external exposure. This report will be devoted to a discussion of these three types and a presentation of illustrative cases.

### URTICARIA

Urticaria, the most frequently seen complication, is the result of a mechanism analogous to that observed in the classic urticaria of serum allergy. Evidence indicates that the acute edematous swelling characteristic of the wheal is due to the increased capillary permeability which follows the release of a histamine-like substance at the subpapillary level of the skin. Evidence indicates that the actual shock cells are located within the walls of the smaller vessels and capillaries in the corium. Patch tests are of no diagnostic value because of the fact that the outer layers of the epidermis are not primarily involved. I observed a typical case of urticaria in a 21 year old German prisoner of war who was receiving intramuscularly 15,000 units of penicillin every four hours during the course of treatment for a chronic osteomyelitis. The wheals appeared on the ninth day and persisted for six days. Intradermal and patch tests with both commercial penicillin (10,000 units per cubic centimeter) and crystalline penicillin sodium G<sup>2</sup> elicited nega-

1 Lyons, C. Penicillin Therapy of Surgical Infections in the U S Army A Report, J A M A **123** 1007-1018 (Dec 18) 1943. Keefer, C S, Blake, F G, Marshall, E K, Jr, Lockwood, J S, and Wood, W B, Jr. Penicillin in the Treatment of Infections. A Report of Five Hundred Cases, *ibid* **122** 1217-1224 (Aug 28) 1943. Barr, J S. The Use of Penicillin in the Navy, J Bone & Joint Surg **26** 380-386 (April) 1944.

2 The crystalline penicillin sodium G was obtained through the Federal Security Agency, Food and Drug Administration, Washington, D C.

tive reactions Crip<sup>3</sup> and Barker,<sup>4</sup> however, reported positive intradermal reactions in each of their cases. That shock organs other than the skin can participate in the reaction is confirmed by the nearly fatal case observed by Price, McNairy, and White.<sup>5</sup> The case of bullous dermatitis due to penicillin reported by Morris and Downing<sup>6</sup> probably was basically an instance of urticaria.

#### ERYTHEMATOVESICULAR REACTIONS

The erythematovesicular group of reactions includes the less clearly defined eruptions appearing within twenty-four hours after intramuscular administration of penicillin is initiated. They involve primarily the groins, hands, and feet, in which areas there frequently has been some previous vesicular eruption suggestive of a dermatophytosis. In the 2 cases reported by Graves and others<sup>7</sup> there appeared within twenty-four hours after the first injection a dyshidrosiform eruption of the hands. In one of these cases the groin and feet manifested a similar but milder eruption. The dyshidrosiform dermatitis in both of these cases appeared in areas which had apparently been sensitized by some type of fungous infection. An intradermal test with commercial penicillin elicited a positive reaction in ninety-six hours in one case but a negative one in the other. The reaction to a patch test in the former was negative. It is assumed that the forearms were used for these tests, although the article makes no direct mention of the sites used. The evidence strongly suggests that this erythematovesicular reaction is closely related to, if not identical with, what dermatologists call a dermatophytid.

CASE 1—A 33 year old soldier had an erythematous-vesicular dermatitis of the groin, scrotum and penis within twenty-four hours of his initial intramuscular injection of penicillin sodium for a crushing injury of a hand. The eruption was first noted after he had received a total of 140,000 units. In a few days the lower part of the trunk and the thighs exhibited a diffuse erythematous reaction which, however, did not go on to vesiculation and exudation, as had the lesion in the groin. The eruption reached its climax on the third or fourth day and, despite continued therapy, desquamation appeared on the sixth day. At this time there also occurred a desquamation of the hands and feet without any preceding cutaneous manifestations. No history of allergy, either familial or individual, was obtained. There had been several acute episodes of dermatophytosis pedis in

3 Crip, L. H. Allergy to Penicillin, *J. A. M. A.* **126**:429-430 (Oct. 14) 1944.

4 Barker, A. N. Allergic Reactions to Penicillin, *Lancet* **1**:177-178 (Feb. 10) 1945.

5 Price, D. E., McNairy, D. J., and White, E. L. Severe Asthma Delayed Sensitization to Penicillin, *J. A. M. A.* **128**:183 (May 19) 1945.

6 Morris, G. E., and Downing, J. G. Bullous Dermatitis from Penicillin, *J. A. M. A.* **127**:711 (March 24) 1945.

7 Graves, W. N., Carpenter, C. C., and Unangst, R. W. Recurrent Vesicular Eruptions Appearing During Administration of Penicillin, *Arch. Dermat. & Syph.* **50**:6-7 (July) 1944.

the past Patch and intradermal tests with commercial penicillin were made both on the normal skin of the forearm and also on the skin of the groin, since this was the site of the penicillin reaction The intradermal test in the right groin elicited a positive reaction, while the other three tests elicited negative ones

CASE 2—Within twenty-four hours after intramuscular penicillin drip was started for a partial intestinal obstruction, a 32 year old soldier manifested a diffuse erythematous dermatitis of the groins, axillas and hands He had received 160,000 units by this time The lesions became vesicular with a tendency to weep centrally and in several days went on to desquamation The feet were only mildly involved This patient gave a definite history of a dermatophytosis in the groins and on the feet but no evidence of an allergic background Patch and intradermal tests with commercial penicillin sodium were carried out as in case 1, again the only positive reaction was that to the intradermal test in the area of the groin Reactions to intradermal and patch tests on the forearm were negative

One of my patients with contact dermatitis (case 3) also manifested the dermatophytid-like type of reaction after a single intramuscular injection

#### CONTACT DERMATITIS

Contact dermatitis as a complication of penicillin therapy is indeed rare if one may judge from the meager reports found in the literature External contact with the allergen in relatively concentrated form is a prerequisite Until recently I felt that contact dermatitis due to penicillin was primarily an occupational dermatosis, since in the cases reported thus far, including my own, the eruption has occurred not in the patients but in the personnel administering the drug The growing popularity of penicillin preparations designed for external use is certain to increase the likelihood of this type of reaction Indeed, it is rather surprising that the dermatologists have not yet reported any cases of contact dermatitis subsequent to topical penicillin therapy However, 3 cases of contact dermatitis of the eyelids have been reported following the use of penicillin in dilute solution as eye drops<sup>8</sup> Similar reports will probably be forthcoming, since the skin of the eyelids is relatively more susceptible to eczematous reactions than is the skin elsewhere Again, it is remarkable that this type of case has not been reported among industrial workers who are in contact with the drug during its manufacture Production methods seem, however, to minimize direct contact with the product

Pyle and Rattner<sup>9</sup> reported the first case of contact dermatitis due to penicillin, and theirs, incidentally, is the only case in which the allergen was definitely proved by patch tests to be crystalline penicillin Binkley

8 Keyes, J E L Penicillin in Ophthalmology, *J A M A* **126** 610-615 (Nov 4) 1944 Selinger, E Dermatitis of the Lids from Penicillin Eye Drops, *ibid* **128** 437 (June 9) 1945

9 Pyle, H D, and Rattner, H Contact Dermatitis from Penicillin, *J A. M A* **125** 903 (July 29) 1944

and Brockmole<sup>10</sup> contributed 2 cases in which the patients were physicians, one of whom had a positive reaction and the other a negative reaction to patch tests with commercial penicillin. The one with the positive reaction was not tested with crystalline penicillin; hence, the exact allergen is unknown. Silvers<sup>11</sup> found that his patient, a research chemist, had negative reactions to patch tests with the pure drug but a positive one to a patch test with the commercial preparation. Barker<sup>4</sup> reported a case in which patch tests with the commercial product elicited positive reactions with no mention being made of patch tests with the crystalline agent.

### Results of Cutaneous Tests

Type of Test	Case 3	Case 4	Controls
Patch tests *			
Commercial penicillin sodium			
Three brands	++	—	— (7 cases)
Fourth brand (new)	++	—	Not done
Fifth brand (new)	—	±	—
(20,000 u per cc)			
Penicillin culture medium†			
Before fermentation	—	—	—
After fermentation	—	—	—
Crystalline penicillin sodium G	—‡	—	—
Intradermal tests			
Commercial penicillin sodium	—	+	— (50 cases)
Crystalline penicillin sodium G	—	—	Not done
Most recently manufactured penicillin sodium	+	+	—

\* All patch tests were made on the forearm and with a concentration of 10,000 units per cubic centimeter of isotonic solution of sodium chloride, unless otherwise noted.

† Culture medium obtained from Eli Lilly and Company.

‡ Negative reaction to patch obtained on normal skin at the site of a previous patch which had elicited a positive reaction, and on the previously erupted area (eyelid).

### ILLUSTRATIVE REPORTS OF CASES

CASE 3—In December 1944 an incision was made and drainage established in both palms of a 41 year old wardman for suppurative cellulitis. The wounds were irrigated with penicillin solution once daily for the two following days, and the patient, through a misinterpretation of an order, received a single intramuscular dose of 10,000 units of penicillin sodium. Within two days there appeared a vesicular dermatitis involving the scrotum, the upper inner parts of the thighs and the interdigital areas of both feet. This disappeared in a week. During the next two months this man intermittently prepared and administered penicillin solution for intramuscular injection to from 1 to 3 patients daily. However, on Feb. 19, 1945 he began to dispense the drug to approximately 45 patients. Three days later there appeared a typical contact dermatitis involving the eyelids, the forehead and the malar prominences. These lesions were characterized by tiny vesicles on an edematous erythematous base and were associated with a mild marginal blepharitis. Three days later while he was evacuating the air from a full syringe some droplets of penicillin solution were inadvertently sprayed into his face. Within several hours his lids became so swollen that the eyes were

10 Binkley, G. W., and Brockmole, A. Dermatitis from Penicillin, *Arch Dermat & Syph* 50 326-327 (Nov.) 1944.

11 Silvers, S. H. Contact Dermatitis from Amorphous Sodium Penicillin, *Arch Dermat & Syph* 50 328-329 (Nov.) 1944.

virtually closed. At this time there were also noted visual fatigue and a mildly pruritic vesicular dermatitis of the dorsal aspects of the third, fourth and fifth fingers of both hands. Penicillin was then suspected and direct contact avoided. The disease subsided rapidly, and a mild desquamation occurred eight days later. Since that episode this man has continued to dispense penicillin to fewer patients without a recurrence of symptoms. Detailed questioning revealed no individual or family history suggestive of allergy. There was a history of a mild focus of "athlete's foot" in the past, but there was no evidence of present activity. The results of various studies on this man are shown in the table. The reactions to patch tests with four commercial preparations of penicillin sodium, including one recently manufactured, were all definitely positive. One recent preparation apparently contained less of the offending antigen, as a patch test with it elicited only a weakly positive reaction. Similar patch tests with crystalline penicillin sodium G and the medium in which penicillin is cultured elicited negative reactions. That the crystalline G fraction was not the allergen was further demonstrated by the negative reaction to the patch test when applied to the site of a previous positive reaction to commercial penicillin and also when applied to the eyelid, the site of the clinical dermatitis. Intradermal tests with the crystalline product elicited negative reactions but elicited positive ones when the commercial preparation was used.

CASE 4—A 34 year old wardsman had been dispensing penicillin intermittently for some months, without symptoms. On Feb 18, 1945 he began to administer penicillin to 45 patients in the same circumstances as in case 3. One day after this mass therapy was begun, there appeared on the eyelids and malar prominences and, to a lesser degree, on the back of the neck an irregular macular dermatitis. This progressed for three days, tending to become vesiculated in the central areas. Again penicillin was suspected and avoided, with a prompt regression of the eruption. In this case too there was no allergic background either individual or familial. Cutaneous tests similar to those made in case 3 were carried out (table). All patch tests with the commercial preparation and the crystalline product elicited negative reactions. However, a patch test with the most recently acquired commercial preparation in a stronger concentration (20,000 units per cubic centimeter) did elicit a positive reaction. The commercial preparations elicited positive intradermal reactions, but when the crystalline product was used the intradermal reaction was negative.

I had occasion to see a third case in which the allergen was not proved but in which the disease was suggestive of a contact dermatitis due to commercial penicillin. The patient was a nurse in whom a mild erythematous, pruritic dermatitis of the eyelids and submental region developed about nine days after she began to give the solution to a greater number of patients. Three weeks later she went on a leave, and the dermatitis disappeared. Patch and intradermal tests with commercial penicillin elicited negative reactions.

#### COMMENT

Certain phases of my studies present interesting questions which warrant further comment at this time. All three types of cutaneous reactions illustrated are of the acquired type, hence, hereditary predisposition apparently is not important. The degree of individual susceptibility, the degree of contact and the period of exposure are all variable factors which combine to determine the clinical severity of the

dermatitis This is most obvious in the group with contact dermatitis The time factor may vary considerably, as shown by the previously mentioned cases of Rattner and Pyle, Barker, and Selinger In both of my cases (3 and 4) the patients were exposed to penicillin for at least two months, but it was only after they began to give penicillin to a greater number of patients that the disease manifested itself clinically When, however, these wardsmen took precautions to minimize direct contact with the solution the disease subsided These 2 cases also demonstrate the difference in individual susceptibility In case 3 positive reactions to patch tests were obtained without difficulty in the concentration of 10,000 units per cubic centimeter, while in case 4 the reaction to the patch test became positive only when the concentration of the solution was doubled The negative reactions to the lower concentration in the latter case merely indicate a milder degree of sensitization and do not thereby exclude commercial penicillin as the etiologic agent

It is now obvious that the mechanism behind the erythematovesicular reactions to penicillin is analogous to that producing the dermatophytid reactions It is known that a number of fungi, including *Penicillium notatum* and the trichophytons, have a common antigenic factor The sequence of events begins with a primary focus in one of the areas susceptible to fungous infection The circulating products of the fungus containing the common antigen then may sensitize the skin of the hands, feet and groin or even the skin of the trunk This sensitization may not become clinically obvious until a later date when adequate exposure to the antigen again occurs This may take the form of an intramuscular injection of penicillin or a reinfection by the original fungus

The erythematovesicular reactions are usually self limited even though penicillin therapy continues uninterrupted In contact dermatitis, on the other hand, the eruption persists or becomes worse as long as the exposure continues Consequently, it is important that penicillin be given early consideration as the etiologic agent of any contact dermatitis involving personnel handling the preparation of the drug The treatment in these cases is obvious

That deliberate sensitization can be produced in a majority of normal human beings has been adequately demonstrated Rostenberg<sup>12</sup> and Welch have produced local sensitization in 9 out of 9 persons given repeated intradermal injections of penicillin solution In a similar manner I was able to confirm this by producing a localized area of vesicular dermatitis on myself after three intradermal injections of penicillin solution at five day intervals This sensitized area could then

12 Rostenberg, A. Ir Local Penicillin Therapy, Arch Dermat & Syph 50 330 (Nov ) 1944



be made to flare up after a patch test with crystalline penicillin sodium G, but not after a control patch with isotonic solution of sodium chloride. This would seem to indicate that the G fraction was the allergen in this particular instance. Subsequently, a single intramuscular injection of 20,000 units of commercial penicillin was followed in nine days by a sudden severe erythematovesicular eruption of all the interdigital areas of both feet. After twenty-four hours, this disappeared almost as dramatically as it had appeared. There was a history in this case of a mild focus of dermatophytosis pedis but of no id reactions at any time. In this instance one is again impressed by the striking similarity of this type of reaction to the dermatophytids.

At this point the question might arise. Exactly what is the allergen in these sensitization phenomena? Penicillin, as it is now available, contains at least five fractions, and there is evidence suggesting that each one of these is specific in its clinical and therapeutic characteristics and possibly also in its sensitizing ability. The clinical and therapeutic effects of the majority of commercial preparations today can be attributed to the G fraction, which is produced so abundantly by the submerged culture method. Even though the newer products are purer, they still contain appreciable quantities of the other fractions and impurities not removed during manufacture. In both of my cases of contact dermatitis patch tests with the crystalline penicillin sodium G and with the medium in which penicillin is cultured elicited negative reactions. Thus one can say only that the allergen is something other than these two constituents. Until the various fractions of the penicillin group are isolated and their roles as allergen clarified, the mechanism of the various sensitization phenomena must remain obscure. The development of a satisfactory penicillin preparation for oral use seems imminent, but this will not obviate the allergic dermatoses, although it may well modify the clinical picture.

Observations on my own cases and a survey of those reported by other authors confirm the opinion that cutaneous tests are of limited diagnostic value in the study of the allergic dermatoses. In contact dermatitis the antigen always reaches the skin by the external route, and therefore the primary changes are in the superficial layers of the epidermis. Consequently, the reaction to the patch test is usually positive. Negative reactions to the patches in these cases would likely become positive if the concentration of the solution were increased or if the patches were left in place for a longer period than the usual forty-eight hours. In the erythematovesicular group the epidermis, too, is the primary level involved. In this group, though the antigen arrives by the hematogenous route, and thus the maximum reaction tends to occur in the deeper layers of the epidermis. Intradermal tests if made in the involved area of skin will probably always elicit positive reactions.

Patch tests usually elicit negative reactions, even when made on the involved skin. In urticaria the shock tissue is in the subpapillary zone, but the deeper layers of the epidermis may be sufficiently sensitized to give occasional positive intradermal reactions. Patch tests are of no value in this group.

#### SUMMARY AND CONCLUSIONS

The three main types of allergic dermatoses complicating penicillin therapy have been discussed and illustrative case reports presented.

Two cases of proved contact dermatitis due to commercial penicillin sodium were observed and studied. Although the exact allergen could not be identified, studies indicated that neither crystalline penicillin sodium G nor the penicillin culture medium was responsible.

Four examples of the erythematovesicular type of reaction were described. An analysis of these cases and the results of tests indicate that the mechanisms behind this erythematovesicular reaction and the dermatophytids are similar and may possibly be identical. The diagnostic value of intradermal tests in this group will be greatly increased if they are made in the dermatitic area rather than on the forearms.

Cutaneous tests are of only limited value in the diagnosis of the three types of dermatitis discussed in this report.

Identification of the exact allergens in these dermatoses must wait until more refined commercial preparations are developed and until the purified penicillin fractions become available for testing.

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## IN VITRO FUNGISTASIS BY A BACTERIUM (BACILLUS SUBTILIS VAR XG AND XY)\*

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AND

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THE POSSIBILITY of successful biologic therapy for fungous diseases has been partially explored by a number of observers. It is of historic interest that the work of Chambers and Weidman<sup>1</sup> antedates by a year the original observations of Fleming<sup>2</sup> on penicillin. They isolated from the apparently normal interdigital toe webs of 4 subjects bacteria which were later identified as *Bacillus subtilis*. When the bacterial colonies were grossly mixed with *Trichophyton gypsum* (*Trichophyton interdigitale*) and this mixture cultured out, there was complete inhibition of fungous growth. Clinical studies using the live culture of *B. subtilis* brought about improvement up to 50 per cent in patients with dermatophytosis. According to Waksman,<sup>3</sup> the growth of many soil fungi is inhibited by species of gram-positive spore-bearing bacilli. In 1942, Katznelson<sup>4</sup> noted that a thermostable, diffusible substance produced by an aerobic spore-forming bacillus inhibited the growth of 71 out of 81 species of parasitic and saprophytic fungi, as well as that of a number of species of gram-positive bacteria.

### INITIAL OBSERVATION

In February 1944, experimental inoculation of three different strains of *B. subtilis* was made on a small central portion of the agar surface.

Aided by a grant from the John and Mary R. Markle Foundation.

From the New York Hospital and the Department of Medicine (Dermatology), Cornell University Medical College.

\*Since the variety of *B. subtilis* is unknown, we have named our organisms XG and XY.

1 Chambers, S. O., and Weidman, F. D. A Fungistatic Strain of *Bacillus Subtilis* Isolated from Normal Toes, *Arch. Dermat. & Syph.* **18**: 568 (Oct.) 1928.

2 Fleming, A. On Antibacterial Action of Cultures of *Penicillium* with Special Reference to Their Use in Isolation of *B. Influenzae*, *Brit. J. Exper. Path.* **10**: 226 (June) 1929.

3 Waksman, S. A. Associated and Antagonistic Effects of Microorganisms, *Soil Sc.* **43**: 51, 1937.

4 Katznelson, H. Inhibition of Micro-organisms by a Toxic Substance Produced by an Aerobic Spore-Forming Bacillus, *Canad. J. Research, Sect. C* **20**: 169 (March) 1942.

of plates already seeded heavily with spores of *T. gypseum*. No inhibition in the growth of *T. gypseum* was noted at any time on 2 of the agar plates. In the third plate one week after the beginning of the experiment there was no evidence of any inhibition in or near the zone inoculated with *B. subtilis*. However, near the edge of the plate a small gray colony was noted, and immediately around this was a clear zone, the remainder of the agar being covered with a profuse growth of *T. gypseum*. The source or nature of this gray colony was unknown. We thought it might have resulted from spores dropping off the loop when *B. subtilis* was seeded on the agar. However, it was difficult to reconcile this possibility with the difference in behavior and the lack of fungistatic ability of the larger inoculum. It seemed more likely that it was a chance contaminant, possibly air borne, which found conditions satisfactory for growth and for the production of an antifungal substance.

#### BACTERIOLOGIC OBSERVATIONS

The micro-organism which produced fungistasis was found to be a gram-positive spore-bearing bacillus. It soon became apparent that the primary isolate, which had a wrinkled surface, consisted of a mixture of a gray growth (which we have named *Bacillus XG*) and of a yellow growth (which we have named *Bacillus XY*). Morphologically these 2 forms of the bacillus were identical. In older cultures, both forms were observed, at times, to dissociate into the other form. With rapid subcultures both the yellow and the gray colonies retained their respective characteristics.

An opinion was expressed by Georges Knaysi<sup>5</sup> that the "two strains belong to the same species. In the position of the spore, spore germination, morphology of the sporangium, etc. the two strains (i.e. the gray and the yellow forms) are almost indistinguishable. The two strains have several characteristics in common with *Bacillus mycoides*, on the other hand, I have not been able to identify them with any yellow pigment-producing bacillus described." Nathan R. Smith<sup>6</sup> considered that "the gray culture is a typical *B. subtilis*, the yellow culture is a variant differing from the gray form only in the production of the pigment. Both forms were present in the original culture. The yellow color is produced only on mediums containing a carbohydrate, thus showing a relationship with *B. subtilis* var. *aterrimus*, which produces a black pigment under the same condition."

<sup>5</sup> Professor of Bacteriology, New York State College of Agriculture, Cornell University, Ithaca, N. Y.

<sup>6</sup> Senior Bacteriologist, United States Department of Agriculture

Since *B. mycoides* is classified by Bergey<sup>7</sup> as a member of the *B. subtilis* group, there was agreement by both authorities that the two forms of our micro-organism (*Bacillus* XG and *Bacillus* XY) belong in the group of *B. subtilis*.

#### PLAN OF INVESTIGATION

This preliminary study was undertaken to determine the effect, if any, of a Seitz filtrate of *Bacillus* XG and XY on the growth of cultures of fungi or of other micro-organisms.

We set out to find the medium best suited to the growth of the bacterium and to determine whether activity of the filtrate depended on variations in the composition of the medium. It was also planned to develop methods for measuring any activity that might appear, as well as for measuring its range of effect on other micro-organisms. Control

TABLE 1—*List of Mediums Tried for Maximum Production of Inhibitory Substance*  
Dextrose was added to each of these mediums in 4 per cent concentration

- 1 Difco neo peptone (lot 364 470)
- 2 Difco proteose peptone (lot 343 490)
- 3 Difco Bacto peptone (lot 369 140)
- 4 Difco Bacto peptone with yeast \*
- 5 Difco tryptase
- 6 Chaussain's peptone (granulated)
- 7 Fairchild's peptone (lot 360 427)\*
- 8 Fischer's peptone (lot 441 295)
- 9 Fischer's peptone + 1 per cent yeast extract
- 10 Beef heart infusion (no sugar)
- 11 Beef heart infusion + 1 per cent yeast extract
- 12 Czapek Dox medium
- 13 Czapek Dox medium + 1 per cent yeast extract \*

\* An adequate concentration of inhibitory substance was obtained in these mediums.

experiments and studies on toxicity were considered essential parts of the study.

#### PRELIMINARY OBSERVATIONS

1 *Culture Mediums*—With beef heart infusion medium, growth of the bacterium was moderate, but the filtrate was inactive. Several other mediums were tried without success. With 4 per cent dextrose and 1 per cent Fairchild's peptone broth, the growth of both strains was moderate. The filtrate of *Bacillus* XG after ten days' growth at room temperature was found to inhibit the growth of several fungi, the filtrate of *Bacillus* XY was inactive. The search for a more favorable medium has continued to this time. Some of the details of the search are recorded in table 1. The highest titer of inhibitory substance has so far been obtained in the filtrate in the Fairchild peptone medium aforementioned. The maximum concentration of inhibitory substance is reached

7 Bergey, D. H., and others. *Bergey's Manual of Determinative Bacteriology*, ed. 5, Baltimore, Williams & Wilkins Company, 1939, p. 645.

in from eighteen to twenty-one days. A satisfactory synthetic medium has not yet been developed.

*2 Measure of Inhibitory Activity of Filtrate* Filtrates of proved fungistatic potency were mixed with fungous spores. This mixture was plated out after fifteen minutes, thirty minutes, one hour and two hours. Fungicidal activity was lacking, since the fungi grew unrestrained.

The fungistatic property of the filtrate was easily demonstrated by dropping 0.2 cc. of the undiluted filtrate on the central part of an agar plate already inoculated with a suspension of the test micro-organism. The area to which the filtrate had been added remained devoid of growth, whereas abundant growth developed over the remainder of the plate, as illustrated in figure 1.

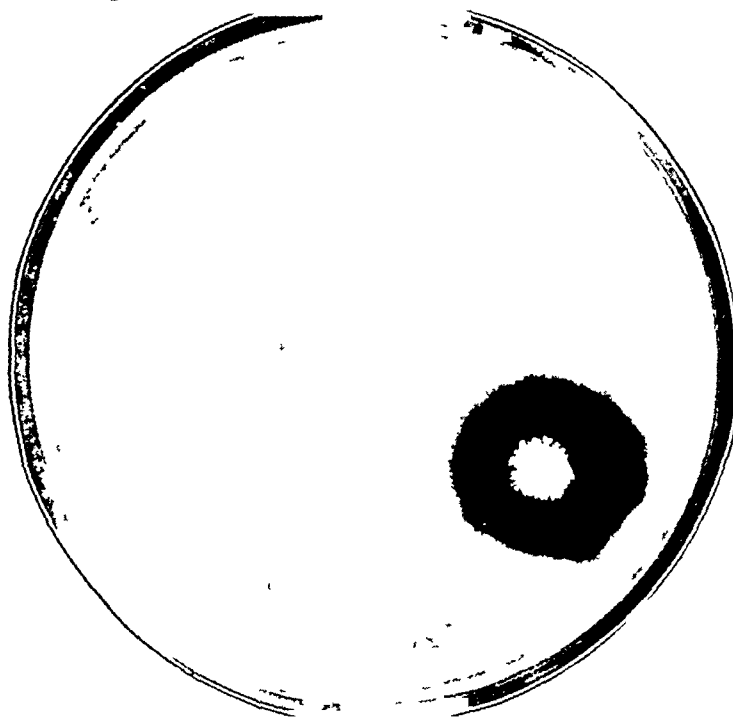


Fig. 1—Original plate showing zone of inhibition around the bacterial growth (*Bacillus subtilis* var. XG and XY) on a plate seeded with *T. gypsum*. The experimental inoculation of *B. subtilis* in the central portion of the growth may be seen indistinctly and without any evidence of fungistasis.

In order to obtain a better idea of the growth-inhibitory potency of the filtrate the following technic was devised. To a measured quantity of melted 4 per cent dextrose agar, certain quantities of both filtrate and test organism were added. This mixture was then incubated at room temperature and observed for at least two weeks. Other dilutions of the filtrate were made, the concentration of the test organism remaining constant. For this reason the result of the control plate represented the maximum growth to be obtained. The suspension of the test fungus was made by pouring 4 per cent dextrose broth over a well developed strain, preferably of granular texture. In order to dislodge the spores, the broth was stirred with a needle until it became cloudy.

Dilutions of the filtrate were made as follows

- 10 cc agar plus 1 cc filtrate
- 10 cc agar plus 0.5 cc filtrate
- 10 cc agar plus 0.1 cc filtrate
- 10 cc agar plus 1 cc of 1/20 dilution of the filtrate
- 10 cc agar plus no filtrate (control)

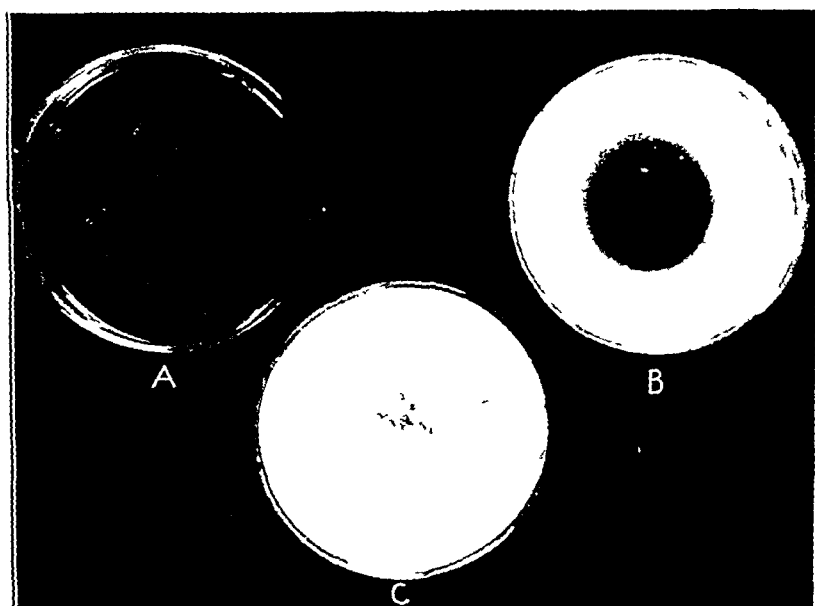


Fig 2—Effect of filtrate of *Bacillus XG* on *T. gypseum*. All three plates contained 10 cc of 4 per cent dextrose agar and the same amount of suspension of viable fungi. In plate A, 1 cc of the filtrate of *Bacillus XG* was incorporated in the agar, with complete inhibition of the fungus. There was 0.2 cc of the filtrate placed on the center of plate B. Plate C, on which no filtrate was placed, served as control. Observation was made after ten days.

TABLE 2—Fungi and Bacteria Inhibited by Filtrate of *Bacillus XG*

<i>Trichophyton gypseum</i>	<i>Scopulariopsis</i>
<i>Trichophyton purpureum</i>	<i>Hormodendron olivaceum</i>
<i>Trichophyton crateriforme</i>	<i>Alternaria</i>
<i>Microsporon audouinii</i>	<i>Chaetomium</i>
<i>Microsporon lanosum</i>	<i>Mycoderma</i>
<i>Microsporon fulvum</i>	<i>Acladium</i>
<i>Monilia albicans</i>	<i>Trichoderma</i>
<i>Sporotrichum schenckii</i>	<i>Torula</i> (pink)
<i>Aspergillus niger</i>	<i>Pneumococcus</i>
<i>Aspergillus nidulans</i>	<i>Bacillus subtilis</i>
<i>Penicillium notatum</i>	<i>Streptococcus hem</i> (C 203)
<i>Fusarium</i>	

The degree of inhibitory effect of the filtrate was designated by the following

- 0—No growth, complete inhibition
- ±—Very scant growth
- | Scant growth
- +| Growth, about half that on control plate, partial inhibition
- ++| Growth intermediate between ++ and +++, slight inhibition
- +++| Growth equal to that on control plate, no inhibition

TABLE 3—Comparison of Inhibition of Growth by Filtrates of Different Bacteria

Name of Fungus or Bacterium	Bacillus XG (Filtrate) Dilution of Filtrate in Agar of Test Medium			Bacillus XY (Filtrate) Dilution of Filtrate in Agar of Test Medium			A T C 6951 (Filtrate) Dilution of Filtrate in Agar of Test Medium			B Mycoides Dilution of Filtrate in Agar of Test Medium			Control No Filtrate Added to This Test
	1/10 1/20 1/100			1/10 1/20 1/100			1/10 1/20 1/100			1/10 1/20 1/100			
	1/10	1/20	1/100	1/10	1/20	1/100	1/10	1/20	1/100	1/10	1/20	1/100	
Trichophyton gypseum	0	0	0	++++			++++			++++			++++
Microsporion fulvum	0	0	0	++++			++++			++++			++++
Monilia albicans	0	0	0	++++			++++			++++			++++
Sporotrichum schenki	0	0	0	++++			++++			++++			++++
Pneumococcus type I	0	0	0	++++			++++			++++			++++
Streptococcus hem C 203	0	0	0	++++			++++			++++			++++
Staphylococcus aureus	0	0	0	++++			++++			++++			++++
Bacillus subtilis	++++	++	+++	0	0	0	++	++	++	++	++	++	++
	0	++	++++	0	0	0	0	0	0	0	0	0	0
The readings in this table were recorded from growths on broth containing dextrose and Fairchild's peptone A commo- the mediums listed in table 1, with similar results for all four filtrates except that less inhibition was observed.													

The readings in this table were recorded from growths on broth containing dextrose and Fairchild's peptone. A comparison was also made, using each of the mediums listed in table 1, with similar results for all four filtrates except that less inhibition was observed with filtrates of Bacillus XG.

TABLE 4—Results of Hemolysis Tests of Heated and Unheated Filtrates on Rabbit and on Human Red Cells

Dilutions of Red Blood Cells	Bacillus XG												B Subtilis Un heated Human Rabbit
	Unheated				65 O for 1 Hr				100 O for 1 Hr				
	Rabbit		Human		Rabbit		Human		Rabbit		Human		
	10	20	100	200	100	200	100	200	100	200	100	200	
1 10	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	0
1 20	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	0
1 40	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	0
1 80	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	0
1 160	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	0
1 320	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	0
1 640	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	0
1 1280	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	0
1 2560	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	0
1 5120	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	0
Key	++++ means complete hemolysis, +++, ++, + and ± denote regressive degrees of redness in supernatant fluid												

Key: +++++ means complete hemolysis, +++, ++, + and ± denote regressive degrees of redness in supernatant fluid, 0 indicates the absence of hemolysis



Bacteriostatic tests against strains of *B. subtilis* and other bacteria were carried out, with use of the same dilution method both in a solid medium and in broth. The mixtures were incubated at 37 C rather than at room temperature. In the tube dilutions, the presence of the inhibitory substance was determined by the absence of turbidity.

The positive results of the dilution test for fungi are recorded in table 2. It was noted that the filtrate of *Bacillus XG* demonstrated a wide range of inhibitory activity among pathogenic fungi and much less inhibitory activity toward bacteria. The filtrate of *Bacillus XY*, on the other hand, was relatively inert toward fungi but did restrain the growth of certain bacteria.

3 *Controls*—The filtrates of six strains of *B. subtilis*, one strain of *B. mycoides* and one strain of *Bacillus coli* failed to show inhibition of fungi (table 3).

4 *Toxic Effect*—As noted in table 4, the filtrate of *Bacillus XG* produces hemolysis of rabbit red blood cells in a dilution up to 1:640 and of human red blood cells in a dilution up to 1:320. After the

TABLE 5—*Effect of Heat on the Fungistatic Activity of a Filtrate of Bacillus XG*

Dilution	Unheated	65 C for 1 Hr	100 C for 1 Hr
1:10	0	0	++++
1:20	0	0	++++
1:100	++++	++++	++++

Key: 0 indicates no change; ++++ indicates complete destruction of the fungistatic activity.

filtrate has been heated at 65 C for one hour there is a slight reduction in the toxic effects (hemolysis up to 1:320 and 1:160 respectively). When the filtrate is subjected to a temperature of 100 C for one hour, the hemolytic effect is greatly reduced (hemolysis up to 1:20 for rabbit's cells and 1:10 for human red blood cells). A similar reduction in hemolysis of both rabbit and human red blood cells is shown for the heated filtrates of *Bacillus XY*.

Comparison of the fungistatic properties of the three filtrates of *Bacillus XG* is presented in table 5. Activity of the filtrate heated at 65 C for one hour is not diminished, but in the filtrate heated at 100 C for one hour inhibitory effect is completely lost. This shows a parallel destruction of the hemolytic principle and of the substance causing the fungistasis.

However, there is probably no correlation between the fungistatic activity of the filtrate and the hemolytic principle since the *Bacillus XY* filtrate exhibits greater hemolytic action, but much less fungistatic effect than the *Bacillus XG* filtrate, in a certain *Bacillus XG* filtrate observed to be relatively inactive as a fungistatic agent the hemolytic

effect was as great as that in filtrates exhibiting normal fungistatic activity

5 *Nature of the Active Filtrate* Preliminary studies indicated that the inhibitory material in the filtrate was produced by the growth of the organism on a medium containing sugar, without dextrose in the medium no inhibitory substance developed. There was satisfactory production when the initial  $p_H$  varied from 5.5 to 7.5. The substance was thermostable, remaining potent after being heated to 60 C for one hour or boiled for fifteen minutes but not after being boiled for one hour. The filtrate was still potent after storage on ice for eleven months.

#### SUMMARY

A micro-organism of the *Bacillus subtilis* group was present as a chance contaminant in an agar plate seeded with *T. gypseum* and was noted to inhibit the growth of this fungus. Several other species of fungi were shown to be similarly susceptible. The inhibitory substance was present in a Seitz filtrate and was potent after storage on ice for eleven months. The filtrate also contained a hemolytic principle. Both the inhibitory substance and the hemolytic principle were destroyed by heating at 100 C for one hour.

66 East Sixty-Sixth Street  
525 East Sixty-Eighth Street  
525 East Sixty-Eighth Street

## RELATION OF QUINACRINE HYDROCHLORIDE TO LICHENOID DERMATITIS (ATYPICAL LICHEN PLANUS)

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AND

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MEDICAL CORPS, ARMY OF THE UNITED STATES

AMONG the many problems and diseases incident to the service of troops in tropical areas during World War II, those relating to the skin have had a prominent place. Of these, the disease which has been called "atypical lichen planus" has been not only one of the most interesting but one of the most baffling from the etiologic standpoint.

Accounts of a cutaneous disease occurring in the Southwest Pacific which resembled lichen planus began to be received in the office of the Surgeon General in the latter part of 1943. Schmitt, Alpins and Chambers<sup>1</sup> and Major Thomas W Nisbet<sup>2</sup> were among the first to recognize the disease and to submit confidential reports of their observations and opinions. Subsequently a number of other reports of independent observations of this disease were received, not only from the Pacific<sup>3</sup> but from other theaters of operation (Mediterranean<sup>4</sup> and India-Burma<sup>5</sup>). The relationship of this disease to the long-continued use of quinacrine hydrochloride (atabrine) was raised in these reports, but because of the difficulties of making controlled observations in the field convincing proof was lacking.

Under the auspices of the Surgeon General, a number of surveys were made and reports prepared<sup>6</sup>. Subsequently, plans for a study

From the Dermatologic Section, Moore General Hospital, Swannanoa, N C

1 Schmitt, C L, Alpins, O, and Chambers, G. Clinical Investigation of a New Cutaneous Entity, *Arch Dermat & Syph* 52:226 (Oct) 1945

2 Nisbet, T W. A New Cutaneous Syndrome Occurring in New Guinea and Adjacent Islands. Preliminary Report, *Arch Dermat & Syph* 52:221 (Oct) 1945

3 Ambler, J V. Letter Report to Chief Surgeon, United States Army, Service of Supply, July 1944. Holbrook, A A. Lichen Planus, Atypical. A Report of Ten Cases, to be published

4 Nelson, L. An Unusual Dermatositis Simulating Lichen Planus and Lichen Cornueus Hypertrophicus, to be published

5 Livingood, C S. Follow-Up Report on Occurrence of an Unusual Skin Disease, Report to Surgeon General, Feb 23, 1945

of the disease, in an effort to determine its cause, course and best method of treatment, were formulated. This report contains the results of such investigations carried on at Moore General Hospital, Swannanoa, N C. During much of the course of the studies, begun in September 1944, the reports referred to previously were not available. Recently a report of observations on 25 cases has appeared.<sup>7</sup>

Before we proceed with the account of these studies, it is necessary to describe the disease under discussion.

Numerous morphologic variants have been described under the name of atypical lichen planus. The lesions noted, though showing numerous variations, have consisted basically of two types: (1) lesions elevated in relation to the surrounding skin and (2) lesions not elevated.

The elevated lesions varied from 2 mm in diameter to large plaques, 30 cm in diameter. They varied in height from a barely perceptible elevation to 1 cm. The color in the beginning was like that of mild erythema, changing in some lesions to bright red and to violaceous, while in others the color progressed only to a dark red and then began to subside. The tops of the lesions were flat, and frequently Wickham's striae were seen. Later the tops were covered with fine silvery scales that were adherent. In the most severe lesions extremely dense grayish scales were present, having a verrucous appearance. In the confluent plaques there were many local variations in height and color.

The nonelevated lesions varied from 1 to 15 cm in diameter. Some consisted of dusky red erythema. Usually the surface had "tissue paper" scaling. As the lesions progressed, telangiectasia usually developed and the skin became atrophic. Pigmentation varied greatly in the atrophic lesions, some showing hyperpigmentation and others depigmentation. Ulceration was not infrequent. Both of the preceding types of lesions were seen in the vast majority of patients, but in the individual patient one type was predominant.

Individual lesions varied greatly in color from pink to dark purple, fading to a brownish color as they became inactive. At this stage some lesions were depigmented at the periphery and hyperpigmented in the center. In some patients showing pigmentation due to quinacrine hydrochloride there was a sharply demarcated area surrounding the lichenoid lesions, varying in size from 0.5 to 2.5 cm, which showed no quinacrine hydrochloride pigmentation.

6 (a) Pincoffs, M C. Atypical Lichen Planus. Present Status of the Problem, Report to Surgeon General Through Theater Surgeon, December 1944. (b) Harvey, A M, Maier J, Papenheimer, A M, Jr, Bang, F B, and Hairston N G. Clinical and Laboratory Studies on Atypical Lichen Planus with Particular Reference to the Role of Atabrine, Report to Surgeon General, Dec 3, 1944.

7 Bagby, J W. A Tropical Lichen Planus-like Disease, Arch Dermat & Syph 52:1 (July) 1945.

On the buccal mucosa and tongue whitish-streaked lesions were common and in cases of severe involvement large thick plaques and occasional ulcerations occurred

In the involved areas sweating was universally absent. In cases of extensive involvement there was generalized hypohidrosis, involving apparently normal skin. The forehead and axillas were, however, exempt from this involvement, and in these areas sweating was unusually profuse. Keratosis of the follicular openings was frequently seen, both associated with lichenoid lesions (lichen spinulosus) and also in areas where no lichenoid lesions were present, being commonest on the upper part of the back and buttocks (keratosis pilaris).

Alopecia in involved areas was common. On return, the hair was usually darker. In 1 case hair returned white but over a period of some four months it returned to normal color. In 3 cases there was associated alopecia totalis.

The nails frequently became lusterless yellow, irregularly ridged and thickened. In cases of more severe involvement there was separation of the distal portion of the nail from the nail bed. In some instances the entire nail was lost.

This description applies to the lichenoid lesions as we have observed them. In many cases there were only such lesions, but in others there were other cutaneous lesions, eczematoid, infectious, exfoliative or ulcerative, which gave a confusing picture. In some cases such lesions were minimal and in others so extensive that it was a question whether the case should be classified as one of "atypical lichen planus with eczematoid dermatitis" or as one of "exfoliative dermatitis with lichenoid lesions." An attempt will be made in the following paragraphs to group and describe these other lesions.

Intertrigo of the genitocrural folds and less frequently, the axillary folds was not uncommon if atypical lichen planus lesions were present in these areas.

Eczematoid lesions were frequently seen and seemed to be of three types. 1 In some cases the initial eruption was an exfoliative eczematoid reaction and the lichen planus lesions usually appeared as the exfoliative dermatitis was subsiding. 2 In other cases there was shown the concomitant development of definite atypical lichen planus lesions and a nummular eczematoid dermatitis. The latter lesions were usually dry and the borders indefinite, with varying degrees of erythema and scaling. 3 The third type of eczematoid reaction was much harder to classify. These lesions occurred in the flexural folds. The majority of these appeared to be intertrigo at the site of lichen planus lesions initially, with secondary infection and a subsequent spreading infectious eczematoid dermatitis. In these cases the lesions were frankly purulent, and follicular pustules were present in the spreading lesions. However, a

relatively small group of flexural eczematoid reactions appeared to be primary eczematoid reactions devoid of the intertriginous and infectious elements

Secondary infection of lesions, especially in the cases of more severe reactions, had been a constant problem. The changes in activity of the sebaceous and sudoriferous glands and ease of trauma are apparently predisposed to infectious complications. The spreading infectious eczematoid dermatitis has been previously mentioned. *Streptococcus pyogenes* and *Staphylococcus aureus* were present in nearly all of these cases. Diphtheroids and *Bacillus coli* were also frequently present. Lymphangitis and lymphadenitis were frequently complications.

Infections of hair follicles, both superficial and furuncular, appeared in most of the cases of severe form and were often fairly extensive. Most of these have been due to *Staph aureus*. In addition, in the elevated hypertrophic lesions, abscesses beneath the lesions due to *Staph aureus* occurred, without apparent follicular involvement or external

TABLE 1—Race

	No. of Patients
White	209
Negro	12
Mexican	7
Filipino	6
American Indian	6
Chinese	1
Japanese	1

abrasion. In the staphylococcic infections, especially of the latter type, phlebitis of adjacent veins occurred in 5 cases.

During the past year over 400 patients with atypical lichen planus have been admitted to Moore General Hospital. Special study sheets were prepared on 314 of these for analysis, from which the following data were collected.

The ages of 288 patients were available. The youngest patients, of whom there were 5, were 19. The oldest patient was 53. Forty-two per cent were between the ages of 20 and 29 inclusive, and 54 per cent were between 30 and 39. The average age of the total group was 32.7 years. Race was tabulated in 242 cases (table 1). Sex distribution was of course meaningless, owing to the nature of the group studied. Early in the year no cases of the disease in women had been encountered; then a few nurses were returned, with the disease, and more recently a considerable number of members of the Women's Army Corps have been admitted.

Complexion, as the term is ordinarily used, was recorded in 259 cases. One hundred and ninety-six, or 82 per cent of the patients were

brunets and 43, or 18 per cent, were blonds. There were 8 patients with red hair and 12 Negroes, who were not included in the percentages. Of 162 patients with schistosomiasis from the Southwest Pacific Area examined as controls 81.5 per cent were brunets and 18.5 per cent were blonds.

The geographic station at the onset of the disease in 293 cases is shown in table 2. Some of the patients had gone directly to the Philippines without having stopped in the New Guinea Area. Place of onset was charted against month of year, and no significant correlations were observed, the number of cases corresponding more to concentration of troops than to month of year.

The geographic location of patients six weeks and six months before onset of the disease showed only one factor that appeared significant. Six weeks before the onset of lichen planus, only 5.9 per cent of 168 patients were in nonmalarious areas (Australia or New Zealand or on ship en route from the United States). Six months before the onset of

TABLE 2—*Geographic Location of Patients at Onset of Atypical Lichen Planus*

	No. of Patients
New Guinea	234
Territory of Papua	65
Territory of New Guinea (British)	63
Dutch New Guinea	54
New Guinea (unqualified)	47
Philippine Islands	18
Bismarck (New Britain)	10
Molukkan (Morotal Island)	10
Solomon Islands	9
Admiralty Islands	6
Australia	5
Thobriand Islands	1

lichen planus, of 197 patients 63.4 per cent were in the United States, Australia, Territory of Hawaii or New Zealand or on board ship en route from the United States. Most patients began taking quinacrine hydrochloride on landing in malarious areas or two weeks before.

A definite history of the duration of suppressive therapy with quinacrine hydrochloride before the initial lesion of lichen planus developed could be obtained in 254 cases. This is shown on chart 1. The cumulative per cent of the total cases in which atypical lichen planus developed and the months of suppressive therapy with quinacrine hydrochloride are shown in chart 2. It is apparent that in only 20 per cent the disease developed within three months, while in 80 per cent it had developed in seven months.

The site of the initial lesion could be determined in 302 cases. Over 80 per cent of the patients had their initial lesions on the extremities. The initial lesions, however, occurred on practically all parts of the body, being present in the mouth, on the scrotum, on the lips, ears and eyelids and in the scalp (table 3). The initial lesion was described by

the patient as an erythema in 35 per cent as a papule in 21 per cent, a vesicle in 12 per cent, and as scaling in 17 per cent of 215 cases

On admission to this hospital, 86 per cent of 262 patients showed pigmented lesions,<sup>8</sup> 59 per cent had lesions on the genitals and 47 per cent buccal lesions. Two hundred and twenty-five (86 per cent) of these 262 patients complained of more or less pruritus. General physical examination did not reveal any consistent visceral abnormality. Sixty

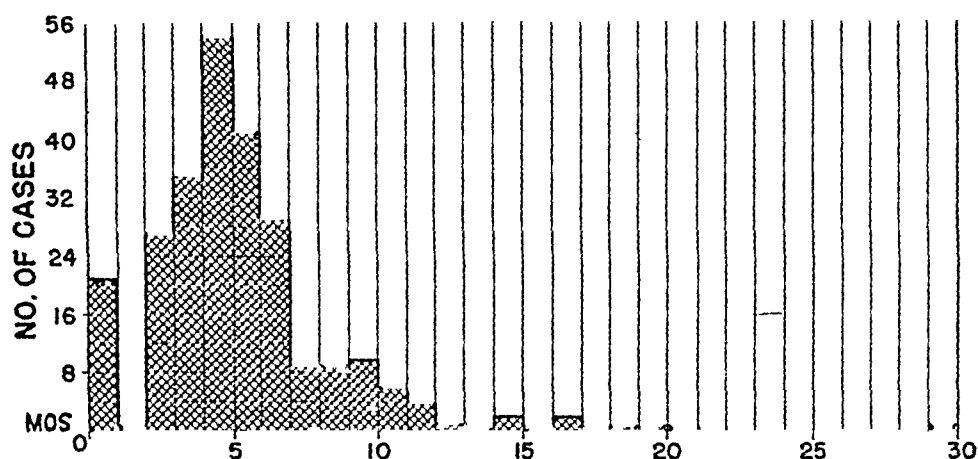


Chart 1—Duration of suppressive therapy with quinacrine hydrochloride before symptoms appeared

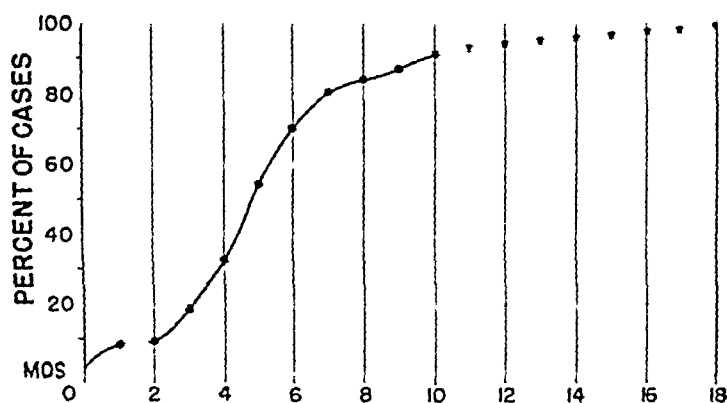


Chart 2—Interval between initiation of suppression with quinacrine hydrochloride and onset of atypical lichen planus in 254 cases

biopsy specimens from early lesions, which were received from overseas, and twenty-five taken at this hospital were examined. No significant differences from descriptions appearing elsewhere<sup>1</sup> were noted. Because of the reports in the French literature of the occurrence of lichen planus lesions in the stomach and bowel, 33 patients were exam-

<sup>8</sup> The pigment has been demonstrated to be melanin by Capt Joseph Jailer (to be reported in detail elsewhere)



med by gastroscopy and 35 by sigmoidoscopy.<sup>9</sup> No lesions resembling lichen planus were seen in the stomach, and only 1 patient showed a lesion in the colon which could have been lichenoid. Roentgen ray examination revealed that the stomach, duodenum and small intestine also were normal in 31 of these patients.

Cases of severe hypoplastic or aplastic anemia associated with lichen planus have been reported from the Southwest Pacific. Four such cases were observed at this hospital, in which 2 patients died. Hepatic function was studied in 35 cases by Captain Lieberthal. The tests used were hippuric acid synthesis, bromsulfalein retention, cephalin-cholesterol flocculation, icterus index and prothrombin time. Three tests in 1 case, two tests in 7 cases and one test in 6 cases revealed abnormal conditions. Only 1 patient showed an abnormal cephalin flocculation reaction. Facilities were not available for estimating the level of vitamin A in

TABLE 3—Site of Initial Lesion

Location	Number of Cases	Per Cent of Cases
Hands and wrists	103	33.7
Feet and ankles	72	23.8
Legs	49	16.2
Groin	12	4.0
Arm	11	3.6
Thigh	9	3.0
Eyelid	8	2.6
Ears	5	1.6
Lips	5	1.6
Face and scalp	5	1.6
Chest	4	1.3
Axilla	4	1.3
Mouth	3	1.0
Abdomen	3	1.0
Neck	3	1.0
Scrotum	3	1.0
All other	3	1.0

the blood or its metabolism. It is recognized that these studies were made several weeks to months after the onset of the disease and after removal of the patients from theaters of operation.

Aside from the few patients with severe anemia mentioned, the hemograms of these patients did not differ from those of other men evacuated from the Southwest Pacific who did not have atypical lichen planus. There were no abnormalities in the urine or stools which differed from those observed in other troops.

After admission these patients showed slow steady improvement in a group of 95 patients, 86 or 91 per cent, stated that improvement had not begun until they had stopped taking suppressive therapy with quinacrine hydrochloride. Of this group 60 per cent had noticed improvement within a month after stopping the drug. In 20 per cent no

<sup>9</sup> These examinations were made by Capt. Milton Lieberthal and will be reported in detail by him.

improvement was noted until they had not taken the drug for two or three months. In 9 cases (9 per cent) the patients stated they had started to improve while still taking quinacrine hydrochloride and while they were still in New Guinea. Of the group not taking the drug when improvement started, 57 were in the United States, 20 en route and 7 still in New Guinea.

Improvement progressed to a point where the lesions were flat, erythema had subsided and only pigmentation remained in from six to nine months in the majority of cases. In many cases atrophy of the skin of the involved areas was present. More prolonged observation will be necessary to establish the duration of lesions and the extent of permanent changes.

The hospital course was by no means always a smooth one. Frequently an infectious pyoderma became superimposed on the lichen planus lesions. In several instances this was further complicated by subcutaneous abscess formation and in 5 cases by thrombophlebitis. Two patients had suppurative phlebitis with blood cultures positive for *Staph aureus*, 1 having in addition a pulmonary embolus. Both recovered after ligation and drainage of the vein.

The routine treatment for these patients consisted only of boric acid baths, a full liberal diet, avoidance of activity which would normally produce sweating and application of a cold cream ointment containing 200 units of penicillin per gram. This provided symptomatic relief as well as prophylaxis against secondary infection.

The large number of patients, however, furnished an opportunity to assay various remedies which had been recommended. Thirty-five patients without significant eczematoid lesions and of roughly the same age and severity of disease were gathered in one ward and treated as follows: (a) 10 (controls) by the routine treatment previously mentioned, (b) 7 with bismuth thio-bismol 0.17 Gm twice weekly for eight injections, (c) 8 with vitamin A 50,000 units as percomorph liver oil every day for thirty days, and (d) 10 with arsenic oxophenarsine hydrochloride 20 mg twice weekly for four weeks. Half of this last group was given a tar paste to apply locally.

In groups (b), (c) and (d) no local therapy was used other than starch baths for pruritus and either cold cream or olive oil for patients with excessively dry skin. Penicillin or other medicines were used only when infection occurred and their use was discontinued as soon as the infection was apparently healed.

Careful observation of all patients at intervals of one week during the course of the experiment and for two weeks thereafter failed to reveal evidence that any of these drugs had any therapeutic effect. All groups showed improvement, but there was no acceleration of the rate of improvement as a result of any one of the several medications used.

At a later date 10 other patients were given 10 per cent British Anti-Lewisite ("BAL") in oil, 1.5 to 2 cc daily for ten days. No effect on the course of the atypical lichen planus was observed.

Many studies made in an attempt to throw some light on the cause of this disease were of no avail and can be disposed of briefly. Bacteriologic cultures of material obtained by biopsy of lesions consistently showed no organism. The usual cutaneous contaminants were present in cultures from the surface of lesions. Pyogenic organisms were recovered from infected lesions. Cultures on Sabouraud's medium from the surface of lesions as well as from biopsies failed to show any pathogenic fungus. Material from twelve biopsy specimens inoculated into fertile hens' eggs failed to show any evidence of the presence of a filtrable virus.<sup>10</sup>

The possible relation of the administration of quinacrine hydrochloride to the development of lichen planus was raised in some of the early reports from overseas. The almost universal history of quinacrine hydrochloride suppression and the common observation that improvement did not begin until the medication was stopped supported this view. Against it was the absence or paucity of cases from other theaters where quinacrine hydrochloride suppressive therapy had been in use and the fact that some patients with lichen planus who had been returned to this country continued to improve even though the suppressive therapy with quinacrine hydrochloride was continued. Further, men with lichen planus who suffered an acute attack of malaria could be treated with the standard seven day quinacrine hydrochloride regimen without exacerbation of their cutaneous lesions. On the other hand, many officers who had served overseas recognized that certain persons were or became sensitized to this drug just as to the sulfonamide compounds and many other drugs, showing an acute eczematoid or exfoliative dermatitis.

Studies were therefore carried out along two lines, first to determine the incidence of cutaneous sensitivity to quinacrine hydrochloride, and second to observe the effect of readministration of the drug to patients whose lichenoid lesions were healing.

Powder for patch tests was made by triturating quinacrine hydrochloride tablets for oral use. Both Squibb and Winthrop tablets were used and tested separately. A small portion of the powder was applied to moistened gauze. This was applied to the skin, covered with cellophane and sealed with adhesive plaster. The readings were made in forty-eight hours. The results were classified as follows: slight, mild erythema +, definite erythema ++, erythematous papule, +++, slight vesiculation +++++, severe vesiculation or necrosis.

<sup>10</sup> Dr. Robert F. Parker, Western Reserve University, made these observations.

One hundred and ninety-eight patients with atypical lichen planus were tested. In addition 100 with schistosomiasis (*Schistosoma japonica*) without cutaneous disease were tested. Both groups had had suppressive therapy with quinacrine hydrochloride previously. The results are contained in table 4. All doubtful tests were excluded. It is apparent that there is no significant difference in the two groups.

Since the reaction of the skin might be due to one of the other ingredients in the tablets rather than to quinacrine hydrochloride itself, a group of patients whose patch tests elicited positive reactions with varying degrees of positivity were tested with the "inert" ingredients of the tablets: (a) Squibb, (b) Winthrop, and (c) Abbott. The results are shown in table 5. While slight to moderate degrees of reaction were seen to these "inert" ingredients, there was no significant grouping of positive reactions to any one of these substances.

Attempts to perform intradermal tests were unsatisfactory because of the acidity of solutions of quinacrine hydrochloride, a 1 per cent

TABLE 4—Patch Tests with Quinacrine Hydrochloride

Disease	Total Number of Patients	Patients with Positive Reactions							
		Squibb Only		Winthrop Only		Both		Total	
		Num ber	Per Cent	Num ber	Per Cent	Num ber	Per Cent	Num ber	Per Cent
Lichen planus	198	11	5.5	10	5.0	20	10.1	41	20.6
Schistosomiasis	100	9	9.0	6	6.0	7	7.0	22	22.0

solution having a  $p_H$  of 4.91 and a 0.1 per cent solution a  $p_H$  of 5.83 (glass electrode). No difference was found in the degree of reaction in 20 patients with lichen planus and 7 controls who had never taken the drug to the intradermal injection of 0.05 cc. of a 1.05, 0.25 or 0.1 per cent solution.<sup>11</sup>

Further efforts were made to demonstrate sensitivity of the skin by the method described by Leftwich<sup>12</sup> for sulfonamide drugs. Serum was obtained from a normal person, the subject was then given 2.8 Gm. of quinacrine hydrochloride in three days and a second sample of serum obtained. Serum was likewise obtained from a patient with malaria who had been receiving suppressive therapy with quinacrine hydrochloride for three months. Patients were then given cutaneous tests with each of these serums. No consistent differences were found in the reactions of 5

11 The solution was made from an ampule of atabrine dihydrochloride, Winthrop.

12 Leftwich, W. B. An Intradermal Test for Recognition of Hypersensitivity to Sulphonamide Drugs, *Bull. Johns Hopkins Hosp.* 74:26 (Jan) 1944.

TABLE 5—Patch Tests with Ingredients of Quinacrine Hydrochloride Tablets for Oral Use

Patch Tests		Quinacrine Hydrochloride *	Starch			Talc			Stearic Acid			Shellac		
			A	B	C	A	B	C	A	B	C	A	B	C
	Squibb	Winthrop												
+	—	—	—	Nd ‡	—	—	Nd	+	—	Nd	—	+	Nd	+
+	—	—	—	Nd	+	—	Nd	—	—	Nd	—	+	Nd	++
+	—	—	Sl	Nd	—	—	Nd	—	—	Nd	—	++	Nd	+
+++	+++	+	Sl	+	—	Sl	+	—	1	+	—	—	—	—
+	+++	+	++	+	+	+	++	—	++	++	++	—	—	—
++	+	—	+	—	—	—	—	—	—	—	—	—	Sl	—
++	+	—	—	Sl	Sl	++	Sl	—	++	Sl	—	—	—	—

\* Not received with the other substances tested Substance used was ampule atabrine dihydrochloride (Winthrop) for intramuscular injections

† Slight  
‡ Not done

TABLE 6—Acute Dermatitis Medicamentosa in Five Patients Convalescing from Lichen Planus Who Were Being Given 0.2 Gm of Quinacrine Hydrochloride Daily

Patient	Age	Onset of Lichen Planus	Drug started	Drug Discontinued	Drug Readministered	Interval Before Onset of Symptoms	"Type of Eruption	Location of Eruption	Blood Quinacrine Level, in Total Micro Gm of grams, Drug Administered	Patch Tests with Quinacrine Hydrochloride		
										Squibb	Winthrop	
G H	39	1/20/44	12/ 7/4	10/10/44	7/ 2/45	4 hours	Erythema, edema, scaling	Generalized	0.6	2.0	+++++	+++++
H B	35	11/ 1/44	8/29/44	12/ 1/44	7/ 2/45	20 hours	Erythema, edema scaling	Generalized	0.8	2.5	++	+
A R	26	8/—/44	9/—/44	9/14/44	7/ 2/4	5 days	Erythema, edema scaling	Flexural folds (axillary, cubital and popliteal) ears	1.4	1.3	++	+
A M	30	12/20/44	11/20/44	2/28/4	7/ 2/45	3 days	Erythema edema, scaling	Axillary, genital folds, crural folds, popliteal	1.4	?	+	+
O G	32	9/—/44	6/ 4/44	?	7/ 2/45	7 days	Erythema, edema, scaling	Presternal genito-crural	5.0	14	++	+

controls and 32 patients in readings made at five minutes, fifteen minutes and at twenty-four hours

Fifty-one patients were selected for study of the effect of readministration of quinacrine hydrochloride. All these patients had had atypical lichen planus with lesions which were predominately lichenoid. All the lesions were clearing and at the time of beginning the test showed only residual hyperpigmentation, atrophy and partial alopecia. All these patients had volunteered after the purpose of the experiment had been explained to them and they had been told that it was possible that their cutaneous lesions would flare up. None of them withdrew during the experiment. After patch tests with two brands of the drug, 0.2 Gm was administered daily. Blood quinacrine hydrochloride levels were estimated at varying periods during the experiment as a check to insure that the patients had been ingesting the drug.

Two definite types of reactions were observed, differing noticeably in type of lesion and in time relationship. In 5 patients an eczematoid type of eruption occurred, characteristically starting as generalized pruritus followed by erythema of the skin, most pronounced in the cubital spaces, popliteal spaces, anterior part of the neck and friction points. In the patients with severer reactions this spread to a generalized red scaling eruption. The eruption had all the characteristics of an acute dermatitis medicamentosa such as is seen in persons who are sensitive to the antisyphilitic arsenical drugs and in persons sensitive to numerous common drugs. The time of onset of symptoms varied from four hours in the patient with the severest reaction to seven days in the one with the least severe reaction. In the 2 with the severest reactions, although the drug had been discontinued after forty-eight and seventy-two hours, the eruption became generalized at the end of the first week, remained static for approximately one week and then slowly subsided. In the next 2 patients, in whom the drug was discontinued after one week, the eruptions did not become generalized but remained principally in the axillary spaces, the cubital spaces, the popliteal spaces and the genitocrural folds with a few indefinite red scaling areas on the trunk. These also subsided promptly after discontinuance of the drug. In the fifth patient, slight scaling about the mouth and a small scaling patch on the thorax about 1 inch (2.5 cm) in diameter were noted at the end of the first week. These remained approximately static for two weeks, although the patient complained of considerable itching. The eruption then spread over the thorax and appeared in the genitocrural folds. The drug was discontinued on the twenty-fourth day and with palliative treatment the lesions improved rapidly and were essentially healed in three weeks.

In none of these patients did the lichen planus lesions show the slightest exacerbation. If anything, they seemed to be less involved in

the reaction than the previously normal skin. All these 5 patients had positive reactions to the patch tests. These 5 patients were removed from the study group (table 6).

The remaining 46 patients continued to take 0.2 Gm. of quinacrine hydrochloride daily. A definite exacerbation of the lichen planus was observed in 9 of these. This was manifested both by the development of new lesions and by the recurrences at the sites of previous lesions. In 6 patients the involvement was extensive, and in 3 only a few lesions were seen. All these lesions showed the characteristics of the original lichenoid eruption. In none was there any evidence of an eczematoid type of reaction. The earliest relapse of lichen planus occurred in twenty-three days and the longest in ninety-seven days. In the majority of cases the time of relapse fell between forty and sixty-three days. The drug was discontinued when a definite exacerbation was observed. Only 2 of these 9 patients showed positive eczematous reactions to the patch tests with the two brands of quinacrine hydrochloride used. Two showed erythema to one brand, and 5 had completely negative reactions. There was no relation between the reaction to the patch test and the severity of the lichen planus eruption (table 7). With the development of typical lesions in these 9 patients, the experiment was terminated. Although none of the rest of the group had shown any blood dyscrasia or constitutional symptoms, it was not believed justified to continue it longer. Of the 37 patients in whom no lesions developed, 20 had taken quinacrine hydrochloride for at least three months and the remainder for approximately sixty days.

The average plasma quinacrine hydrochloride level in the patients in whom exacerbations developed was 35 micrograms per liter when the drug was discontinued, and the range was 22 to 65 micrograms. In those in whom exacerbations did not develop the average was 38 micrograms per liter on discontinuance and the range 10 to 84 micrograms.

In view of these observations, it is felt that two definite types of cutaneous reactions are seen as a result of the administration of the drug in certain susceptible persons.

One type is an acute sensitivity reaction beginning within ten days, characterized by diffuse erythema and edema in the flexural folds. When severe it continues to a generalized exfoliative dermatitis. This reaction can occur and become extremely severe with small doses of quinacrine hydrochloride and a very low blood level. In this group of patients positive reactions to patch tests with quinacrine hydrochloride are to be expected.

The second type is localized, or "fixed," and morphologically resembles lichen planus. Prolonged administration of the drug is apparently necessary to elicit this reaction. Of 254 patients with atypical lichen planus who were questioned, only 49 (19.3 per cent)

TABLE 7—*Exacerbation of Lichen Planus in Nine Patients Covealescing from Lichen Planus Who Were Being Given 0.2 Gm of Quinacrine Hydrochloride Daily*

Patient	Age	Onset of Lichen Planus	Drug Started	Drug Dis continued	Drug Readministered	Interval Before Onset of Symptoms	Type of Eruption	Location of Eruption	Total Gm of Drug Administered	Blood Quinacrine Level, in Gm of grams, When Discontinued	Patch Tests with Quinacrine Hydrochloride	
											Squibb	Winthrop
P G	23	6/1/44	2/24/44	8/1/44	7/2/45	23 days	Purple papules, site of quiescent lesions	Feet, hands fore arms, legs, trunk	60	65	0	0
T C	24	8/25/44	4/27/44	12/29/44	7/2/45	32 days	Localized purplish scaling papules	Extremities, trunk, face, scalp	108	95	+	0
G I	20	10/15/44	9/1/44	4/29/45	7/2/45	40 days	Localized purplish scaling papules	Velvet, Wrist	108	32	0	0
L A	24	11/15/44	10/25/44	3/29/45	7/2/45	45 days	Localized purplish scaling, atrophic and papular	Face, ears, trunk, extremities	112	30	0	0
F O	20	3/1/45	5/27/44	6/2/45	7/2/45	52 days	Purple scaling papules	Chest, iliac region	110	22	+	+++
G Sh	31	4/25/45	1/1/45	5/12/45	7/19/45	63 days	Purple confluent scaling papules	Face, extremities, trunk	108	29	+	0
G Se	20	10/—/44	3/—/45	3/—/45	5/19/45	87 days	Purple scaling papules	Trunk, extremities, Forearms, legs	126	34	0	0
P S	18	10/20/44	7/—/44	11/20/44	5/19/45	97 days	Purple papules, scaling	Inner aspect of thighs	152	36	++++	+++
	33	12/—/44	6/—/44	3/—/45	5/19/45				192	32	0	0



stated that their eruption began within three months of the initiation of suppressive therapy with quinacrine hydrochloride. Of the 46 patients in this experiment 19.5 per cent showed exacerbation of the lichen planus on readministration of the drug for sixty to ninety-seven days. Thus the percentage of patients in the experimental group who had an exacerbation of their disease within three months was practically identical with the percentage of the larger group studied clinically in whom the disease had developed within the same period after they had started quinacrine hydrochloride.

The etiologic importance of quinacrine hydrochloride in the production of atypical lichen planus was emphasized by Schmitt<sup>1</sup> in an early report, and the question was discussed by many others, both in written communications and in informal conferences. In favor of the association were (a) the absence of any reports or records of the disease in New Guinea and adjacent areas before occupation by American and Australian troops, (b) the increased incidence when suppressive dosage was increased and discipline more rigidly enforced and (c) the usual failure of patients to improve until the drug was stopped. Against an etiologic relationship were (a) the lack of reports of a comparable number of cases of the disease from other theaters where suppressive therapy with quinacrine hydrochloride was in effect, (b) the relatively long period that many men had been receiving suppressive therapy with quinacrine hydrochloride before the disease developed, (c) the failure of typical patients to show exacerbation of lichenoid lesions when given a therapeutic course of the drug for an acute attack of malaria and (d) the gradual improvement of some patients although continued on the usual suppressive dosage of 0.1 Gm. daily.

During this time it was recognized, as mentioned before, that in certain persons there developed a sensitivity to quinacrine hydrochloride as manifested by a positive reaction to a patch test and the development of eczematoid lesions on administration of the drug for therapeutic or other purposes. The crucial test had to be of the development of new lichenoid lesions on readministration of the drug under conditions which would, so far as possible, exclude the participation of other factors. Harvey and others<sup>6b</sup> working in New Guinea, reported exacerbation in twenty-four to seventy-two hours in 7 of 9 patients on readministration of the drug. In 6 of these, however, the exacerbation was described as oozing or crusted.

Among the cases reported in this paper are several from other theaters where suppressive therapy with quinacrine hydrochloride in varying doses had been in force for varying periods throughout the year. Suppression with quinacrine hydrochloride in the Southwest Pacific area was continued throughout the year and after the spring of 1943 the dose was 0.7 Gm. or more weekly. This is a higher dose and

more continuous administration than was in force in other theaters. The comparative number of patients with lichen planus who had not taken the drug observed at this hospital has been no greater than that seen in civilian dermatologic practice. Two patients with lichen planus have been returned from overseas who had had the condition in civilian life, and a nurse who had never been overseas contracted the disease.

As has been previously pointed out, when quinacrine hydrochloride was readministered to a group of convalescent patients with atypical lichen planus two distinct types of reactions were encountered.

One of these, occurring in from four hours to seven days, was eczematoid in nature and was not accompanied with the development of new lichenoid lesions or recrudescence of old ones, and all patients had positive reactions to patch tests with quinacrine hydrochloride. This is believed to be similar to the eczematoid eruption seen in some persons without lichen planus on ingestion of the drug.

The other reaction, occurring in twenty-three to ninety-seven days after readministration of quinacrine hydrochloride, consisted in the development of typical lichenoid lesions at new and at old sites, was not accompanied with any eczematoid characteristics and in the majority of patients was accompanied with a negative reaction to a patch test. Lichenoid lesions developed in 46 patients (19.5 per cent) within approximately three months of the administration of the drug, which is almost identical with the original incidence of development of the disease, 19.3 per cent within three months. We regard this as strong evidence of an etiologic relationship of "atypical lichen planus" to the prolonged ingestion of relatively large quantities of the drug.

This belief, however, does not explain the mechanism of the action of quinacrine hydrochloride or dispose of all the problems. The fact that no exacerbation of lichenoid lesions was observed in less than three weeks accounts for the impunity with which the drug may be administered for an acute attack of malaria. The long incubation period may also explain the failure of several observers to see exacerbations when the drug was readministered to a small group for a few days or weeks. We have no satisfactory explanation, however, for the improvement of 7 to 10 patients who were in a malarial study group and continued to take 0.1 Gm daily for one hundred and fifty days. The other 3 patients with atypical lichen planus in this group failed to improve at the expected rate. This group was observed during the winter months, and while supposedly on the same dosage on which the disease originally developed received only half the amount daily of the experimental group. The relationships of plasma quinacrine hydrochloride level, diet, climate and possibly other accessory factors in the developments of the disease have not been studied.

The occasional occurrence of lichen planus after long-continued administration of bismuth or arsenic preparations may be comparable to its development after quinacrine hydrochloride. The addition of quinacrine hydrochloride to these drugs invites speculation on the cause of "idiopathic" lichen planus.

#### SUMMARY AND CONCLUSIONS

Clinical observations in 400 cases of atypical lichen planus are described.

Reactions to patch tests with quinacrine hydrochloride in patients with atypical lichen planus showed no significant difference from those in a control group.

Therapy with bismuth, oxophenarsine hydrochloride (mapharsen), vitamin A and "BAL" was of no benefit.

Readministration of quinacrine hydrochloride caused two types of lesions, (a) early acute eczematoid reaction in 98 per cent, (b) late chronic lichenoid reaction identical with original lesions in 19.3 per cent.

The exacerbations of atypical lichen planus on experimental readministration in 46 cases occurred in the same frequency within three months as they had, according to history, in 254 cases on initial ingestion of the drug.

Quinacrine hydrochloride is an essential etiologic factor in the production of the "atypical lichen planus" occurring in American troops overseas.

These cutaneous reactions following the ingestion of quinacrine hydrochloride in a small percentage of persons are far outweighed by the military value of the drug in suppressing *Plasmodium vivax* malaria and curing *Plasmodium falciparum* malaria.

## COMPLICATIONS OF LICHENOID DERMATITIS

Glomerulonephritis and Severe Pigmentary Changes in the Exfoliative Stage of Lichenoid Dermatitis

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FROM New Guinea and its neighboring islands a large number of cases of the severe generalized lichen planus type of lichenoid dermatitis with decided pigmentation have been observed. As yet little has appeared in the literature on this disease, but in the near future much will doubtless be published<sup>1</sup>. The case being presented had several unusual features which are of significance.

### REPORT OF A CASE

Early in September 1944 the patient, a 31 year old artillery lieutenant, was admitted to the hospital. He had no past history of cutaneous disease or renal trouble of any type. He was in good health in February 1944, when he landed in New Guinea. According to his history, he took quinacrine hydrochloride, 0.2 Gm daily for the prevention of malaria for the next five months. Early in June 1944 he noticed a peeling of the skin of his hands, with underlying redness. This eruption spread in a few weeks to involve the entire body, and while this occurred the lesions assumed a violaceous hue. A few days later the skin of his entire body began to ooze fluid, and he was hospitalized on June 29, 1944. He then noticed that his skin was scaling considerably, and while at first the diagnosis had been lichen planus he was then considered to be suffering from exfoliative dermatitis. At this time the patient observed that his skin was getting dark, that his urine had a dark brown color and that his axillary and inguinal lymph nodes had become swollen and tender. He was evacuated to the United States and was admitted to the hospital to which we were assigned early in September 1944.

Physical examination disclosed that his entire skin had a dark brown "coffee" color, associated with a coarse generalized exfoliative dermatitis. The flexor

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1 The following articles appeared since this paper was submitted for publication: Bagby, J. W. Tropical Lichen Planus-like Disease, *Arch Dermat & Syph* **52**: 1 (July) 1945. Livingood, C. S., and Dieuaide, F. R. Untoward Reactions Attributable to Atabrine, *J A M A* **129**: 1091 (Dec 15) 1945. Bereston, E. S. Lichenoid Dermatitis, *J Invest Dermat* **7**: 69, 1946. Lutterloh, C. H., and Shallenberger, P. L. Unusual Pigmentation Developing After Prolonged Suppressive Therapy with Quinacrine Hydrochloride, *Arch Dermat & Syph* **53**: 349 (April) 1946.

areas and the ears were oozing, while elsewhere the exfoliative process was dry. Many small black irregular areas of pigmentation were scattered widely over the body. The inguinal, axillary and cervical lymph nodes were discretely enlarged and firm. The liver and spleen were palpable. The patient had a temperature of 100.8 F, a pulse rate of 120 and a respiratory rate of 22 on admission. For six days his disease ran a febrile course with a maximum temperature of 102.6 F. He was toxic and lethargic at this time. Overseas the patient's urine had been normal on repeated tests, however, at this time 12 to 15 red blood cells per high power field were seen in the urine, and albumin (2 plus) was present. The sedimentation rate was 80 mm per hour, hemoglobin content 58 per cent, red blood cell count 2,810,000 and white blood cell count 13,100. Roentgenograms of the chest showed normal conditions, and the adrenal glands were normal. The nitrogen level at this time was 20 mg and the nonprotein nitrogen level 36.3 mg per hundred cubic centimeters.

Figure 1 presents laboratory observations throughout the course of the disease. Biopsy of an inguinal lymph node and its adjacent skin revealed on gross examination that the skin was irregularly pigmented and that the lymph nodes were enlarged and grayish black. On section the lymph nodes were dark gray, the color being due to cortical pigmentation. The pigment did not give the prussian blue reaction for iron. Microscopically the pigment in the nodes appeared as dark brown coarse granules both extracellular and intracellular. Intracellular pigment was found within phagocytic cells only. In the skin the major portion of the pigment was in the papillary portion of the corium. In addition, there were inflammatory changes in the skin, consisting of a severe edema of the epidermis and corium, a lymphocytic infiltration located high in the papillary portion of the corium with 3 to 5 eosinophils per high power field, atrophy of the stratum corneum and stratum lucidum and loss of the basement membrane, separating the epidermis from the corium, with exfoliation of superficial portions of the stratum corneum.

The blood pressure was always within normal limits. The specific gravity of the urine was between 1.010 and 1.015. Repeated examinations of the urine revealed no melanin. A tentative diagnosis of lichen planus with exfoliative dermatitis and mild secondary infection was made at this time, although the possibility of a nevocarcinoma was also considered.

The patient was given 100,000 Oxford units of penicillin intramuscularly daily for five days, and within forty-eight hours after institution of this therapy his temperature dropped to normal, where it remained. He was given two blood transfusions because of his anemia. Treatment administered consisted of a high vitamin high caloric diet, ferrous sulfate orally, colloidal baths, compresses of solution of boric acid applied to moist areas and boric acid ointment to all other areas. The patient's general condition improved, exfoliation diminished, and oozing subsided. The urinary abnormalities, however, persisted and were constantly observed in daily samples. By Sept. 22, 1944, the nonprotein nitrogen was 76.9 mg and the urea nitrogen 45 mg per hundred cubic centimeters. Granular and pus casts appeared in the urine, in addition to the red blood cells and albumin. Because of the persistent urinary abnormalities, a retrograde pyelogram was made which was normal. It was felt that the patient had a toxic glomerulonephritis secondary to his lichen planus and exfoliative dermatitis. During the next three months the patient's weight, which had been 30 pounds (13.6 Kg.) below normal, returned to normal, and his cutaneous pigmentation faded gradually, leaving many irregular dark brown and black pigmented areas as well as a general dusky tint to the skin. The exfoliation ceased entirely. The urine still showed

microscopic hematuria, although the specific gravity rose to 1020 late in October. Anemia gradually disappeared during this period, and the urea nitrogen and nonprotein nitrogen returned to normal. In February 1945, five months after admission, the patient was in excellent condition, except for residual

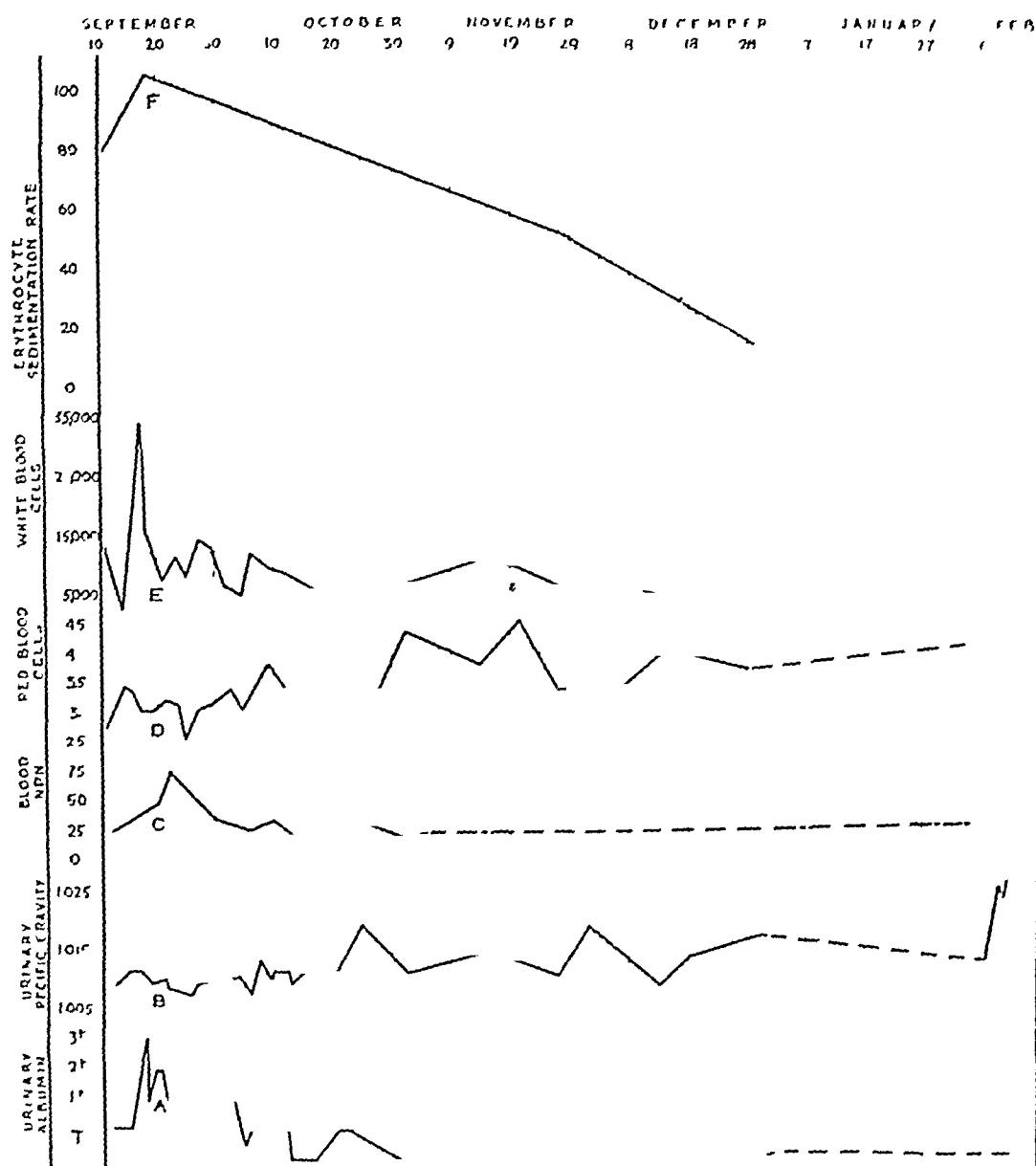


Fig 1—Curve *A* presents the urinary albumin levels, varying from 0 to 3 plus. Curve *B* indicates the variations in specific gravity in repeated samples of urine. It is noteworthy that for the first forty days the specific gravity was well fixed and only after that time showed some variability and increased ability to concentrate. Curve *C* represents the nonprotein nitrogen level of the blood in milligrams per hundred cubic centimeters. The normal level is considered to be 35 mg. Curve *D* depicts the red blood cell count in millions of red blood cells per cubic millimeter. For the first forty days there was a rather profound anemia following which there was slow but consistent improvement. Curve *E* shows the white blood cell counts. For the first thirty days there was evidence of leucocytosis. Curve *F* shows the erythrocyte sedimentation rate according to the Westergren method. The normal level is up to 20 mm in one hour.

irregular areas of pigmentation scattered over the body and a slight generalized darker tint to his skin than existed prior to his illness (fig 2)

#### COMMENT

This case is presented primarily because of the appearance of the glomerulonephritis during the course of the lichen planus type of lichenoid dermatitis with associated exfoliative dermatitis. Glomerulonephritis is not mentioned in any of the standard texts<sup>2</sup> as following

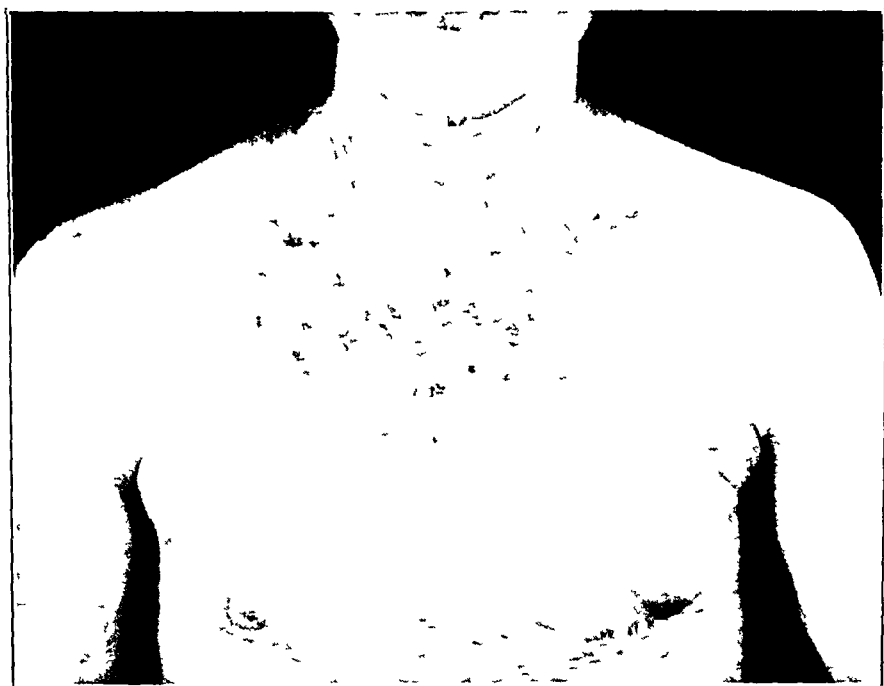


Fig 2—Residual pigmentation of skin

either lichen planus or exfoliative dermatitis, and no reference is made to such a sequence in the literature for the past ten years. The severe diffuse melanin pigmentation involving skin and lymph nodes is a second unusual factor in this case. Although pigmentation is often reported both in lichen planus and following exfoliative dermatitis, the severity seen in this case was most unusual. Futcher<sup>3</sup> reported 11 cases of glomerulonephritis following cutaneous infections such as impetigo and

2 Sutton, R. L., and Sutton, R. L., Jr. *Diseases of the Skin*, ed 10, St Louis, C. V. Mosby Company, 1939. Cecil, R. *A Text Book of Medicine*, ed 6, Philadelphia, W. B. Saunders Company, 1943. Fishberg, A. M. *Hypertension and Nephritis*, ed 4, Philadelphia, Lea & Febiger, 1939.

3 Futcher, P. H. *Glomerular Nephritis Following Infections of the Skin*. *Arch Int Med* **65**: 1192 (June) 1940.

infected wounds. Hayman and Martin<sup>4</sup> in reviewing 76 cases of nephritis from the literature reported that in 41 per cent the inflammations followed infections. Secondary infection of the skin in the case which we are reporting was mild, lasted for only a few days and involved only small areas of the body. Diffuse melanin pigmentation of the skin and lymph nodes in a case of exfoliative dermatitis was reported by Goedhart<sup>5</sup> in a case report which makes no mention of previous cases in the literature. His description of the pigmentary changes in the skin and lymph nodes on biopsy parallels that in our case, although glomerulonephritis was not observed in his case and was present in ours. The role of quinacrine hydrochloride in the production of the cutaneous lesions in our case must be considered in view of the evidence recently accumulated.<sup>6</sup> Whether the renal abnormalities are also due to quinacrine hydrochloride in this case is undetermined.

#### SUMMARY

A case is reported of the generalized severe lichen planus type of lichenoid dermatitis associated with exfoliative dermatitis in which there occurred glomerulonephritis and decided melanin pigmentation of the skin and lymph nodes. The role of quinacrine hydrochloride in this disease is mentioned.

#### CONCLUSIONS

1 Glomerulonephritis may be a complication of the lichen planus type of lichenoid dermatitis associated with exfoliative dermatitis.

2 Severe generalized melanin pigmentation of the skin and lymph nodes may accompany the lichen planus type of lichenoid dermatitis associated with generalized exfoliative dermatitis.

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4 Hayman, J. M., Jr., and Martin, J. W., Jr. Acute Nephritis. Review of Seventy Seven Cases. *Am J M Sc* **200** 505 (Oct.) 1940.

5 Goedhart, C. Dermatose exfoliative avec pigmentation melanique cutanee et envahissement pigmentaire des ganglions lymphatiques (reticulose lipomelanique de Pautrier-Woringer), *Ann de dermat et syph* **10** 316 (April) 1939.

6 Reactions Attributed to Atabrine. Circular Letter 441, Office of Surgeon General, Washington, D. C., July 19, 1945.



## EXFOLIATIVE DERMATITIS DUE TO POLYVALENT ARSENICAL SENSITIVITY

Report of a Case

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**A** DERMATITIS following therapy with a trivalent arsenical is rarely followed by a similar intolerance to a pentavalent arsenical, such as tryparsamide<sup>1</sup>. However, a polyvalent sensitivity must be considered in all cases, especially in the case of patients with a previous arsenical dermatitis.

A mild dermatitis following tryparsamide was first reported in 1924, and treatment was continued without further intolerance<sup>2</sup>. Dermatitis of severer or of exfoliative nature has been reported<sup>3</sup>. Milder dermatoses were observed by others<sup>4</sup>. Urticarial reactions,<sup>5</sup> fixed drug

1 (a) Stokes, J H, Beerman, H, and Ingraham, N R, Jr. Modern Clinical Syphilology, ed 3, Philadelphia, W B Saunders Company, 1944, p 1044 (b) Moore, J E, and others. The Modern Treatment of Syphilis, ed 2, Springfield, Ill, Charles C Thomas, Publisher, 1943, p 105

2 Ebaugh, F G, and Dickson, R W. The Use of Tryparsamide in Treatment of General Paralysis. Results of First Year's Experience, J A M A **83** 803-807 (Sept 13) 1924

3 Skoog, A L. Tryparsamide Therapy in Neurosyphilis, J Missouri M A **22** 387-390 (Oct) 1925 Bragman, L J. Tryparsamide Dermatitis. Report of a Case and Survey of the Literature, Am J Syph & Neurol **18** 308-310 (July) 1934 Nair, V G. Exfoliative Dermatitis After Tryparsamide, Indian J Ven Dis **3** 13-14 (March) 1937 Epstein, E. Sensitivity to Both Trivalent and Pentavalent Arsenicals, Arch Dermat & Syph **36** 964-969 (Nov) 1937 Golz, H H. Sensitivity to Arsenical Drugs. Report of an Unusual Case Exhibiting Sensitivity to Both Trivalent and Pentavalent Arsenic, Am J Syph, Gonorr & Ven Dis **23** 344-347 (May) 1939 Moore and others,<sup>1b</sup> p 125

4 (a) O'Leary, P A, and Becker, S W. Further Observations on Treatment of Neurosyphilis with Tryparsamide, M J & Rec **123** 305-308 (March 3) 1926 (b) Phelps, J R. Reactions Incidental to the Administration of 191,778 Doses of Neoarsphenamine and Other Arsenical Compounds in the U S Navy, U S Nav M Bull **27** 205-223 (Jan) 1929 (c) Robinson, S S. Dermatitis Due to Tryparsamide. Report of a Case, Arch Dermat & Syph **34** 251-252 (Aug) 1936 (d) Kopp, I, and Solomon, H C. The Untoward Reactions of Tryparsamide, Am J Syph, Gonorr & Ven Dis **24** 265-283 (May) 1940 (e) Beerman, H, and Shaffer, B. Reactions to Tryparsamide. A Review of Ten Years' Experience, Brit J Ven Dis **16** 145-165 (July-Oct) 1940 (f) Downs, W G, McDermott, W, and Webster, B. Reactions to Tryparsamide Therapy, Am J Syph, Gonorr & Ven Dis **25** 16-21 (Jan) 1941

5 Kampmeier, R H. Urticaria Due to Tryparsamide, Arch Dermat & Syph **44** 671-673 (Oct) 1941 Kopp and Solomon<sup>4d</sup>

eruptions,<sup>6</sup> papular dermatitis,<sup>7</sup> herpes zoster<sup>8</sup> and onychoptosis<sup>9</sup> have also been noted

A review of the few reported cases reveals that an exfoliative dermatitis following use of tryparsamide had been preceded by a dermatitis due to a trivalent arsenical in 67 per cent of the cases. The use of patch tests following the tryparsamide dermatitis indicated polyvalent sensitivities in all patients tested. However, fixed, papular and urticarial eruptions were more frequently manifested initially with tryparsamide therapy and patch tests usually elicited negative reactions. In the case reported herein there was exhibited a polyvalent arsenical sensitivity of fifteen years' duration.

#### REPORT OF CASE

A 47 year old moderately obese white woman had secondary syphilis in 1929 and received intravenous injections presumably of neoarsphenamine, for approximately eight months. At that time there developed a severe exfoliative dermatitis including loss of hair and nails. No further treatment was given until 1944, when following positive results of serologic tests and an examination of the spinal fluid she was given about three months of bismuth therapy. The diagnosis was late meningovascular neurosyphilis.

She was then given 0.04 Gm. of oxophenarsine hydrochloride on Jan. 29, 1945, not having disclosed on questioning at that time the history of exfoliative dermatitis in 1929. Within eight hours there was a generalized erythema, pruritus and facial edema. This was followed by a scarlatiniform eruption, vesiculation on the neck and, later, a dry, branny desquamation of the neck, trunk, arms and palms. The skin was normal again within three weeks. There were no other toxic manifestations, results of urinalyses were normal and the patient was confined to bed only two days.

A recheck of the spinal fluid made one month later revealed group II abnormalities and a positive serologic reaction of the blood. Further bismuth therapy was given until on April 19 an injection of 0.5 Gm. of tryparsamide was made. Again within eight hours a generalized erythematous, pruritic dermatitis was present, although clinically milder than that following the injection of the oxophenarsine hydrochloride. This was followed by a maculopapular morbilliform eruption especially prominent on the neck and face and with edema of the

6 Robinson, H. M. Fixed Dermatitis Due to Tryparsamide, *Am J Syph* **17** 507-509 (Oct.) 1933. Kemp, J. E., and Menninger, W. C. Fixed Eruption Due to Tryparsamide. Report of a Case, *Am J Syph & Neurol* **19** 195-196 (April) 1935. Pillsbury, D. M. Fixed Arsenical Eruption. Sensitivity to Tryparsamide at Sites of Pigmentation Following Dermatitis Due to Silver Arsphenamine, *Arch Dermat & Syph* **34** 103-106 (July) 1936. Underwood, L. J. Nitritoid Reaction Following Tryparsamide Therapy, *ibid* **51** 313-315 (May) 1945. Kopp and Solomon.<sup>4d</sup>

7 Ellis, F. A. Tryparsamide Dermatitis, *Am J Syph, Gonorr & Ven Dis* **22** 336-339 (May) 1938.

8 Rosenberg, W. A. Bilateral Asymmetrical Herpes Zoster (Following Tryparsamide Therapy), *Illinois M J* **74** 164 (Aug.) 1938.

9 Silverston, J. D. Tryparsamide Therapy in Neurosyphilis, *Lancet* **2** 693-699 (Oct. 2) 1926.

face and hands. Later there was bianny desquamation involving especially the trunk, neck, palms and soles. Within five weeks the skin was normal.

There was no other manifestation of toxicity except slight fever for two days, the patient remaining ambulant. Visual signs or symptoms were not present. Treatment for the dermatitis consisted of colloid baths, soothing lotion and ointment and intravenous injections of calcium gluconate, sodium thiosulfate and dextrose. There was no personal or family history of allergy, nor has the patient had other eruptions.

Patch tests with oxophenarsine hydrochloride, dichlorophenarsine hydrochloride, neoarsphenamine, sulfarsphenamine, bismarsen and tryparsamide on August 9 all resulted in pruritus, erythema, edema, vesiculation or bullae within twelve hours at the sites of the patches. The most pronounced reactions occurred from neoarsphenamine, oxophenarsine hydrochloride and dichlorophenarsine hydrochloride. A similar concentration of arsenicals was tested on 4 other patients, 1 of whom had had a previous mild erythematous arsenical dermatitis. All had negative reactions.

#### SUMMARY

A polyvalent sensitivity to arsenicals was present fifteen years following a severe exfoliative dermatitis. It was manifested by a mild exfoliative dermatitis after one injection of oxophenarsine hydrochloride and three months later after an injection of tryparsamide.

The use of patch tests may give useful information concerning patients with a previous arsenical dermatitis. Those manifesting strong positive reactions should not have further arsenotherapy.

## CUTANEOUS LEISHMANIASIS (ORIENTAL SORE)

Report of Autochthonous Cases Observed in Haifa

S GILL, M D

HAIFA, PALESTINE

THE first autochthonous cases of cutaneous leishmaniasis occurred in Haifa in the year 1936. They came from a densely populated Arab quarter, and the dissemination of the disease during the first years was observed entirely in this quarter and in the neighboring houses. Today one sees patients from different parts of the town, and their number has already exceeded 300.

In this country the insect vector for the parasite called *Leishmania tropica* is *Phlebotomus papatasi*, according to Adler and Theodor. As this species of sandfly is widely distributed in the area, dissemination of the peculiar dermatosis can be expected if the new repellents and insecticides will not eventually prevent the spread of any insect-borne disease.

Since Haifa became an area of endemic cutaneous leishmaniasis no increase in the number of sporadic cases of visceral leishmaniasis (kala-azar) has been observed.

### GENERAL DESCRIPTION

The autochthonous cases of leishmaniasis cutis are from the beginning as varied as they usually are in the old endemic areas.

The number of patients I treated was 87. The youngest of them was 7 months old, the oldest 64 years.

The baby had *Leishmaniasis mutilans auriculi*. More than half of her left outer ear had been lost before I saw her. Coagulation with diathermy once applied destroyed all the parasites, and the wound was definitely healed within some weeks.

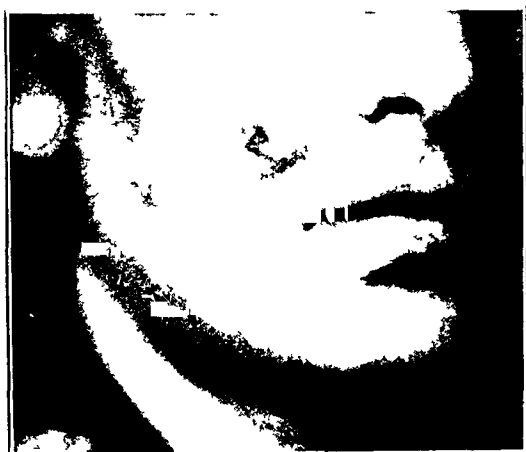
Two patients had ulcerated boils on the lower lip. In such cases the following possible diagnoses should be considered: diphtheria ulcerosa, *ulcus phagedenicum*, syphilis, tuberculosis, blastomycosis and cancer. But typical of leishmaniasis was a narrow periulcerative infiltration of rather firm consistency and apple-jelly color.

The material for microscopic examination was taken from an infiltrated border, not from the ulcerated part. For this purpose I used a pen. Immediate fixation in methyl alcohol and staining with fresh Giemsa solution for forty minutes gave clear slides.

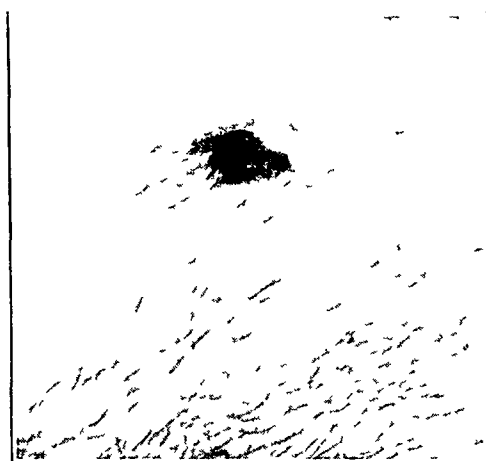
A tendency to verrucous growth was observed in 2 cases. In both the lesion was resistant to treatment for a long time, and 1 of the patients had a relapse after years of apparent healing.

Three patients had the lesions in the form of a linear infiltration, which was flat and glabrous.

A large impetiginous plaque developed in 1 case.



1 Oriental sore of three months' duration. This is a typical granuloma in the initial stage of ulceration.



2 Oriental sore of two months' duration in a man aged 30. It is a small ulcerated nodule unusually located on the hypogastrium.

A cheloid-like boil was once observed.

In 2 patients there was a single small ulcerated node similar to those which I saw in some recurrences.

One such nodule had an unusual location on the hypogastrium of a man.

In 3 cases there were multiple ulcers on the legs, resembling at first sight diphtheritic ulcers



3 *Leishmaniasis nodularis* Relapse occurred two years after apparent healing of an ordinary boil



4 *Leishmaniasis cutis verrucosiformis*

In 2 patients the parasites spread from the primary granuloma in the lymphatic vessels, forming a short chain of small subcutaneous nodules (nodular lymphangitis)

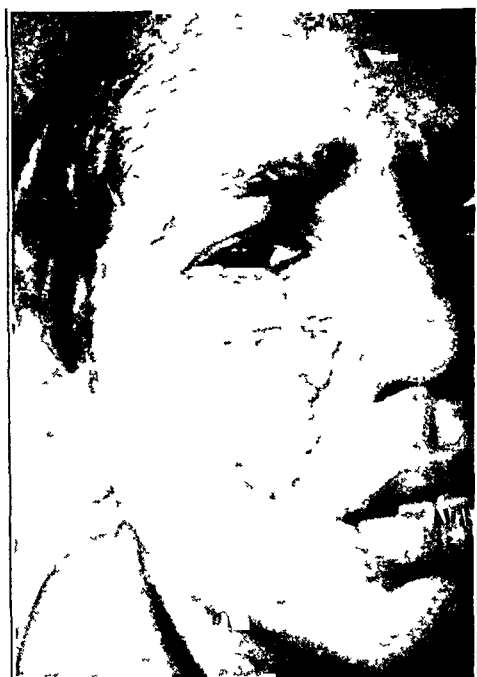
In the remaining cases there were typical granulomas—some with a squamous surface and some ulcerated

In 1 patient the number of boils was 93

Cases of spontaneous healing of the boils could not be observed, as the greatest part of infected persons were undergoing some kind of treatment

#### TREATMENT

I used a 10 per cent solution of quinacrine hydrochloride or emetine hydrochloride, for impregnation of the involved tissues, and when the number of boils was great, intramuscular injections of lithium antimonythiomalate



5 The same case as that in figure 4 Appearance of leishmaniasis serpiginosa five years later

Physical therapy consisted of application of diathermocoagulation and roentgen rays

The best therapeutic results seemed to be obtained from irradiation with roentgen rays, but for the greater part of the patients in the Hadassah-Polyclinic this kind of treatment was inaccessible

#### RELAPSES

Eight lesions relapsed One of them was initially a verrucosiform leishmaniasis, which resisted roentgen irradiation and apparently healed

after repeated impregnations with quinacrine hydrochloride. But five years later a creeping extension of relapsing leishmaniasis began.

In the initial stage 7 patients had ordinary granulomas.

Three varieties of relapses were observed.

They were the same types as have been reported by Gitelson in Russia<sup>1</sup> and by Dostrovsky in Palestine:—(1) leishmaniasis nodularis—small apple-jelly nodules which arose in the different parts of the scar tissue and in the immediate neighborhood (5 cases), (2) leishmaniasis serpiginosa—a creeping patch extending into the former intact skin from a part of the scar (1 case), (3) leishmaniasis orbicularis—small papules in the borders of a scar, forming a closed irregular circle (1 case).

The last case presented a combination of discrete nodules and serpiginous patches.

In all these lesions I looked for parasites but found them in only 3 cases—in 2 of the nodular and in 1 of the serpiginous variety.

For the relapses in my cases I blame not only the inadequate potency of the drug but also its inaccurate application.

In successful treatment the entire tissues involved must be impregnated with the drug. But sometimes under the pressure of the injected fluid the "boil" broke through and a part of the fluid escaped. Or the needle was inserted too deeply under the lesion and some of the drug was not applied in the right place.

As a result of such inaccurate application not all parasites came into contact with the drug and a part of them were not destroyed—probably only weakened.

In the hard terrain of the scar tissue the parasites began to multiply again—sometimes after years of inactivity.

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1 Gitelson, I. I. Atypical Form of Cutaneous Leishmaniasis, *Sovet vestnik venerol i dermat* (no. 5) 1:34, 1932.

2 Dostrovsky, A. Leishmania Recidiva of the Skin, *Harefuah* 8:1-11 (May-June) 1934.



## DERMATITIS DUE TO QUINACRINE HYDROCHLORIDE

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THE presence of our troops in strength in the regions of endemic malaria in the Southwest Pacific has presented opportunity for the extensive clinical use of quinacrine hydrochloride, U S P (atabrine). Its use as a suppressive agent has been enthusiastically described in lay and scientific literature. Its popularity as a therapeutic agent is steadily rising. A moment of reflection for appraisal of any possible side effects may be appropriate.

During the past two years, in excess of 2,000 patients who have recently been evacuated from the Pacific area with some type of dermatologic problem have been seen. Among these soldiers, fungous infections, various forms of cutaneous pyodermas, severe pustular and cystic acne and various types of eczematoid eruptions were the most frequent conditions found. Several patients were seen with conditions which, it is believed, represented cutaneous reactions to quinacrine hydrochloride. This may be more widespread than is generally accepted so that a description of the clinical courses in 2 cases may be merited.

Quinacrine hydrochloride is the 3-chloro-7-methoxy-9-(1 methyl-4-diethylamino) butylamino acridine. It is a yellowish green fluorescent dye and has been widely used since 1935 in the treatment of malaria. Many physicians now prefer it to quinine because of its "low toxicity" and usually it is better tolerated by most patients. Quinacrine hydrochloride is more effective than quinine on the sexual phase of the parasites especially the gametocytes of *Plasmodium falciparum*. My colleagues and I have used this drug during the past year in terminating therapeutic malaria which was used in the treatment of neurosyphilis in over 300 cases. Reactions to quinacrine hydrochloride in these soldiers have been minimal and include anorexia, nausea, vomiting, abdominal cramps, diarrhea, headache, vertigo, hyperhidrosis and mental symptoms. The last have consisted principally in mild excitement, nervousness and restlessness which improve rapidly after the drug is discontinued. A few instances of mental confusion, delusions and hallucinations have been reported.<sup>1</sup>

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1 Gaskill, H S, and Fitz-Hugh, T, Jr. Toxic Psychoses Following Atabrine, Bull U S Army M Dept, March 1945, no 86, p 63

A cutaneous eruption caused by quinacrine hydrochloride has been described by Noojin and Callaway.<sup>2</sup> They reported a case of exfoliative dermatitis which developed in a diabetic patient who received quinacrine hydrochloride for malaria. After administration of the drug was discontinued, the skin improved. Subsequently, a positive reaction to a patch test, which also produced an exacerbation of the cutaneous eruption, was obtained. Storey<sup>3</sup> recorded the case of a generalized, erythematous, papular eruption which developed in a person with malaria who was treated with quinacrine hydrochloride. Two days after the drug was discontinued the rash faded.

Several distinct types of dermatoses were frequently seen among the soldiers returning from the Southwest Pacific, and they were so similar that a common cause was suggested. This causative factor was an extremely puzzling problem for some time. One type of eruption consisted of violaceous papules, which frequently became confluent to form plaques, some of which became thickened and hypertrophic. The lesions developed on any part of the body but had a predilection for the extremities. Several cases of generalized involvement resulting in exfoliative dermatitis were observed. The mucous membrane showed grayish white patches on the tongue and oral mucosa in some cases. When the eruption healed, there remained a mahogany pigmentation identical to that seen following lichen planus. Because of the similarity in its cutaneous, morphologic and histologic appearance, the eruption was frequently termed "atypical lichen planus" or "a tropical lichen planus-like disease" (Bagby<sup>4</sup>). Schmitt, Alpins and Chambers,<sup>5</sup> from their close observation of soldiers with this condition, were of the opinion that this disease was the result of a sensitivity to quinacrine hydrochloride. Mitchell,<sup>6</sup> in discussing Duemling's paper, had reached a similar impression. Bagby<sup>4</sup>, however, in a recent paper on this subject, did not favor this etiology and stated the belief that additional factors must be involved.

An eczematoid dermatitis, involving frequently the hands and feet but occurring on any part of the skin, was the second and commoner type of eruption seen. The patients usually stated that at the onset,

2 Noojin, R. O., and Callaway, J. L. Generalized Exfoliative Erythroderma Following Atabrine. Report of a Case, North Carolina M. J. **3** 239 (May) 1942.

3 Storey, W. E. Toxic Exanthema Following Prolonged Atabrine Administration and Resembling Brill's Typhus Fever, J. M. A. Georgia **27** 317 (Aug) 1938.

4 Bagby, J. W. A Tropical Lichen Planus-Like Disease, Arch. Dermat. & Syph. **52** 1 (July) 1945.

5 Schmitt, C. L., Alpins, O., and Chambers, G. A Clinical Investigation of a New Cutaneous Entity, Arch. Dermat. & Syph. **52** 226 (Oct) 1945.

6 Mitchell, J. H., in discussion on Duemling, W. W. Cutaneous Diseases in the South Pacific, Arch. Dermat. & Syph. **52** 75 (Aug) 1945.

small pinhead-sized vesicles developed along the sides of the fingers, the thumb and index finger frequently being the first involved. Shortly thereafter, on the dorsum of the hands and feet, patches of vesicular, coin-sized weeping areas developed. Other parts may be involved, such as the palms, wrists, extremities, scalp, ears, neck, groin and, less often, areas on the trunk. At the time these patients came under our observation their lesions consisted of coin-sized patches of weeping, crusted plaques, which frequently became confluent, especially on the hands and feet. The cause in such cases had always been a problem until the patient described in case 2 was observed.

All the soldiers with this condition had certain similar clinical findings besides their cutaneous lesions. They had spent six months or more in the tropics of the Southwest Pacific, with the intense heat and humidity, where adverse hygienic conditions existed. In general, the average loss in weight was from 20 to 35 pounds (9 to 16 Kg). Their skin was dry, and many had follicular keratosis, especially about the elbows and shoulders. All stated that they received no fresh dairy products, and the only butter was a canned vegetable oil. This diet undoubtedly could produce mild deficiencies in vitamin A. No determination of the blood level of this vitamin was made. All persons had also had quinaquine hydrochloride for suppressive therapy for several months or longer.

It was our policy to culture and scrape all these lesions for fungi. Most of these examinations resulted in negative findings. On some patients, fungi were demonstrated from interdigital and toe nail lesions. In view of Hopkins' <sup>7</sup> report, the possibility that these could be *id* lesions was considered, but the response to fungicidal therapy to the focus and bland therapy to the *id* lesions was not so prompt as would be expected in ordinary circumstances.

In spite of various means of treatment, the lesions usually took from thirty to ninety days to heal and were benefited only after the patient had discontinued taking quinaquine hydrochloride, had regained his normal weight and had been given additional vitamin A. Schmitt <sup>8</sup> described this type of dermatosis as "bilateral eczematoid dermatitis," which he believed was a result of intolerance to quinaquine hydrochloride. In four months he was able to observe over 200 such cases, 4 of which he reported in detail. These cases were discussed with S. W. Becker, <sup>9</sup> who was of the opinion that cutaneous lesions which developed as

<sup>7</sup> Hopkins, J. G., Hillegas, B., Camp, E., Ledin, R. B., and Rebell, G. Treatment and Prevention of Dermatophytosis and Related Conditions, Bull. U. S. Army M. Dept., June 1944, no. 77, p. 42.

<sup>8</sup> Schmitt, C. L. Bilateral Eczematoid Dermatitis—A Manifestation of Drug Intolerance, to be published.

<sup>9</sup> Becker, S. W. Personal communication to the author.

the result of a sensitivity to quinacrine hydrochloride were similar to those seen from the arsphenamines, namely, lichenoid lesions, vesicular-bullous dermatoses, exfoliative dermatitis and a fixed type of drug eruption. Duemling reported 3 cases of exfoliative dermatitis which he alleged were produced by quinacrine hydrochloride and in which positive reactions to patch tests were obtained with a saturated solution of this drug.

It is my purpose to report 2 cases, the first of which illustrates the urticarial or fixed type of drug eruption from quinacrine hydrochloride and the second the vesicular-bullous-eczematoid type of reaction.

#### REPORT OF CASES

CASE 1—A 34 year old private first class was admitted to the Finney General Hospital on Jan 7, 1945. He had arrived in the Southwest Pacific April 22, 1944, at which time he began taking quinacrine hydrochloride as a suppressive measure,  $1\frac{1}{2}$  grains (0.09 Gm) ten times weekly.

Cutaneous lesions first developed in July 1944 which consisted of multiple itching and inflammatory vesicles along the sides and backs of the fingers. The eruption gradually spread involving the back of the legs, with itching and persistent urticaria-like wheals. His condition necessitated hospitalization on August 28. The eruption was resistant to therapy until the administration of quinacrine hydrochloride was stopped on September 20, following this there was a gradual improvement. This soldier had several attacks of chills and fever in the Southwest Pacific subsequent to the discontinuance of quinacrine hydrochloride. On one of these occasions malaria was found, and the patient was treated with quinine, without any exacerbation of his previous cutaneous eruption.

On admission to Finney General Hospital, this patient showed mahogany-colored, hyperpigmented, quarter-sized patches scattered over the backs of the hands, the anterior surface of the forearms and the posterior aspect of the legs. There was no evidence of active dermatitis. The patient was given a fifteen day furlough on Jan 25, 1945, during which period he had chills and fever. At this time he took quinine, without any cutaneous reaction, and returned to the hospital February 9. While awaiting transportation to a convalescent hospital, he had another chill, on February 20. A malaria smear was positive for *Plasmodium vivax*, and the patient was given quinacrine hydrochloride, 3 grains (0.19 Gm) every six hours. The next day the patient noticed an intense itching eruption, especially on the legs and the backs of the hands, which were the sites of the previous cutaneous lesions. He stated that this was similar to the dermatitis he had previously experienced. Examination revealed an urticaria-like eruption on the backs of the thighs. The hands showed edema, vesiculation was present along the sides of the fingers and an erythematous eruption was diffusely spread over the backs of the hands and fingers. The administration of quinacrine hydrochloride was discontinued. The blood level was 0.001 mg per hundred cubic centimeters. Tests for sensitivity to light were performed. Exposures were made with an ultraviolet lamp at a 12 inch (30.4 cm) distance for variable periods, from five to twenty seconds. No increased sensitivity to light was demonstrated. Daily examinations showed a resolution of the dermatitis after the patient had been given quinine. There was a small amount of scaling, and the urticarial lesions were still present but less intense. One week later the erythematous and edematous wheals had faded, leaving the previous areas of hyperpigmentation.

present A patch test with 2 per cent quinacrine hydrochloride was performed, but the reaction was negative at the end of forty-eight and seventy-two hours

CASE 2—A 42 year old chaplain, who entered military service on May 5, 1941, stated that he had had an eruption on his back in 1930 and 1932, which was diagnosed as psoriasis He had been a resident of Florida since 1923 and had been free of cutaneous eruptions from 1932 until this episode He arrived in the Southwest Pacific area on March 17, 1944 and began taking quinacrine hydrochloride for suppressive therapy on March 1, 1944 He took ten  $1\frac{1}{2}$  grain (0.09 Gm) tablets a week In August numerous small vesicles developed along the sides of his fingers, which were accompanied with some swelling Throughout his illness, he never experienced any lesions or discomfort on his feet He was treated in the dispensary with compresses of solution of aluminum acetate Some slight improvement occurred He arbitrarily decreased his dosage of tablets of quinacrine hydrochloride to six a week Shortly thereafter, lesions developed on his legs, groin, elbows, ears and scalp, for which he was hospitalized on October 25 Two weeks later all administration of quinacrine hydrochloride was discontinued, and the patient began to show gradual improvement, but because of the chronicity of his condition he was evacuated, he arrived at Finney General Hospital Jan 1, 1945 At this time, all his lesions had regressed and consisted only of dry, scaling patches on the vertex of the scalp, behind the ears, elbows, hands, groin and legs There was some pitting present on all the nails, and the disease was thought to be psoriasis in a state of involution He was, therefore, given a thirty day leave and 5 per cent ammoniated mercury ointment was prescribed for local therapy While at home, he experienced a chill and, after several days, consulted his family physician, who made a diagnosis of malaria and instituted quinine therapy, consisting of 10 grains (0.65 Gm) a day for ten days

He returned to the hospital February 6, at which time his eruption was completely well Because of his history, a malaria smear was made, which revealed *P. vivax*, and therapy with quinacrine hydrochloride was instituted, consisting of 3 grains (0.19 Gm) every six hours for five doses The next day he noticed a redness and itching of the previously involved areas of skin He, however, continued to take quinacrine hydrochloride, taking a  $1\frac{1}{2}$  grain (0.09 Gm) tablet three times a day The next day the hands were swollen and reddened, and numerous small vesicles were present along the fingers Both elbows were covered by acute erythematous, edematous patches, as were the legs, ears and groin

The administration of quinacrine hydrochloride was discontinued, and 10 grains (0.65 Gm) of quinine were given three times daily for a week The skin was treated by compresses of solution of aluminum acetate and calamine lotion The lesions gradually improved, and after ten days they consisted of dry, scaling patches The serum level of quinacrine hydrochloride, taken on the third day after it was administered, was 0.005 mg per hundred cubic centimeters Reactions to patch tests with 2 per cent solution of quinacrine hydrochloride and 5 per cent ammoniated mercury ointment were negative His tolerance to exposure to ultra-violet light showed a normal response of erythema at ten and fifteen seconds A solution of 2 per cent quinacrine hydrochloride was painted on his skin, and further exposures to light were made, without any appreciable change

A letter was received from this patient on August 13, in which he stated that he had an attack of malaria in April and again in July, for which he had received quinine without any untoward reactions In June, an infection of the bladder developed for which he was given sulfathiazole, which produced within

twelve hours a similar eruption to that previously caused by quinacrine hydrochloride. He immediately discontinued taking the drug, and the skin, after peeling for a few days, was of normal appearance a week later.

# COMMENT

In both of these patients dermatitis developed on the hands and extremities which had its onset while the men were on suppressive therapy with quinacrine hydrochloride. For three months the cutaneous lesions resisted all means of therapy, until the administration of quinacrine hydrochloride was discontinued. After this the skin became much improved, and in case 1 it was healed except for some post-inflammatory hyperpigmentation. The patients were given convalescent furloughs during their first week of hospitalization, and while at home both had chills and fever, for which they received quinine, without any reactions of their skin.

The question naturally occurs as to whether these cutaneous lesions were the result of the malarial infection. In my observation of malaria as a therapeutic agent including 564 patients admitted during the past twelve months to the Neurosyphilis Center of Finney General Hospital, the dermatologic complications encountered have been herpes simplex, herpes zoster and urticaria. In a review of the literature<sup>10</sup> the only other type of cutaneous manifestation described was a bullous dermatitis, reported by Davis.<sup>11</sup> This healed after antimalarial therapy. In both of these cases the eruption persisted for some time, even after the parasites were absent from the blood, in contradistinction to urticarial lesions from malaria which disappear when the parasitemia ends.

As quinacrine hydrochloride is an acridine dye, one would expect that it could be a photosensitizing agent. This is further suggested by the occurrence of the lesions on the backs of the hands, forearms and legs. Sensitivity tests to ultraviolet irradiation, however, in both cases showed a normal reaction time. Whether natural sunlight would have any effect was not determined. We have, however, been encouraging sun bathing by our patients convalescing from malaria who have received quinacrine hydrochloride without incident to date.

In the case reported by Noojin and Callaway, a positive reaction to a patch test was found. The percentage of the drug utilized in making these tests was not recorded. Both of my patients gave negative reactions to a 2 per cent solution of quinacrine hydrochloride. This result, however, would be expected in this type of reaction, where the sensitized tissue lies in the dermis and not in the epidermis.

10 Bhowmick, S. K. Malarial Urticaria—Two Case Reports, *Indian M. Gaz.* **78** 48 (Jan.) 1943. Nayudu, R. V. N. Malaria and Its Treatment by Synthetic Remedies. Atabrine and Plasmochin, *ibid.* **72** 531 (Sept.) 1937.

11 Davis, A. G. Tertian Malaria with Unusual Type of Skin Manifestation, *J. A. M. A.* **103** 286 (July 28) 1934.

From a clinical standpoint, the cutaneous lesions which occur after the development of a hypersensitivity to quinacrine hydrochloride are similar to those seen from the arsphenamines and the sulfonamide drugs. Chemically they are all aromatic organic compounds and are closely related to coal tar derivatives and aniline compounds. This was exemplified in case 2, in which the dermatitis produced by quinacrine hydrochloride and sulfathiazole were identical.

The development of cutaneous reactions to quinacrine hydrochloride should in no way reflect on the usefulness of this drug in the treatment of malaria. The incidence of this hypersensitivity is extremely infrequent and occurred in probably less than 0.2 per cent of persons who took quinacrine hydrochloride regularly in the Southwest Pacific. One, however, should be cognizant of the various types of cutaneous sensitivity which may develop, so that they may be recognized early and other antimalarial remedies substituted.

#### SUMMARY

1 Two cases of a vesicular-eczematoid type of drug eruption which are believed to be due to quinacrine hydrochloride (atabrine) are reported.

2 The initial reaction occurred overseas. Relapses of the malaria occurred in this hospital. Within forty-eight hours after the institution of therapy with quinacrine hydrochloride all areas previously involved became acutely inflamed. Following further therapy with quinine and bland local treatment, improvement occurred rapidly and healing was complete.

3 The possibility of the drug's having some photosensitizing effect was considered, because it is a fluorescent dye. However, this could not be demonstrated in these 2 cases.

4 It is suggested that if eczematoid, vesicular, bullous, lichenoid, urticarial or exfoliative dermatitis develops in persons receiving quinacrine hydrochloride a possible sensitization to this drug should be considered.

The Duluth Clinic, Duluth, Minn

## Clinical Notes

### AN ILLUMINATING MAGNIFIER FOR THE READING OF THE RAPID TEST FOR SYPHILIS

F RAPPAPORT, PH D., AND F EICHHORN, TEL AVIV, PALESTINE

The difference between positive and negative tubes used in our rapid test for syphilis<sup>1</sup> may seem sometimes of insufficient sharpness to the inexperienced eye. The source of difficulty is the strong Tyndall phenomenon exhibited by the non-flocculated antigen sometimes complicating the interpretation of results<sup>2</sup>

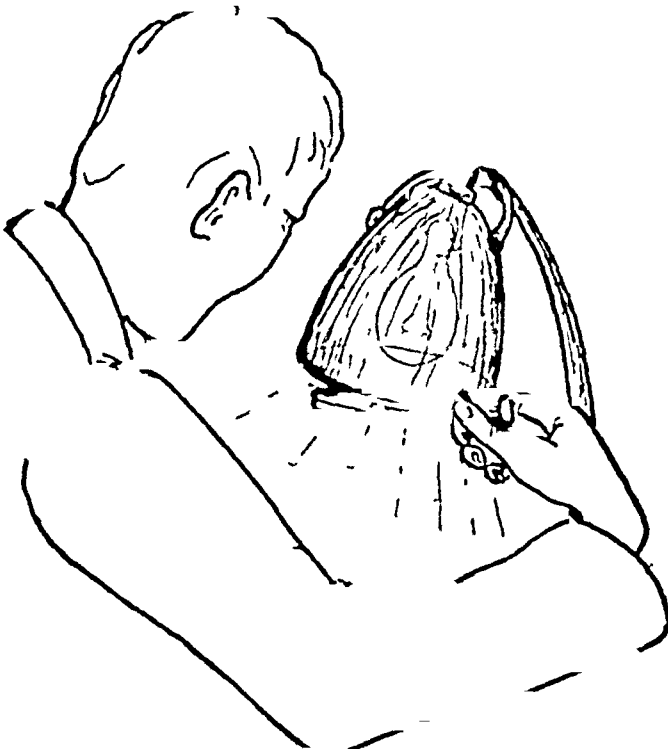


Fig 1—Diagram showing tube held almost horizontally against rim of lamp shade and examined from above with top of table as background

This possible source of error can be easily eliminated by centrifugation of the test tubes, thus increasing the size of flocculi, before the results are recorded. Very light tubes which do not have to be balanced are preferable for this manipulation.

From the Beilinson Hospital Petach-Tikva and the Municipal Hadassah Hospital

1 Rappaport, F, and Eichhorn, F. Rapid Test for Serodiagnosis of Syphilis, *Lancet* **1** 426 (April 3) 1943, **2** 599 (Nov 4) 1944

2 Hewish, E A, and Barritt, M M. Rapid Macroflocculation Test for Syphilis. Method of Rappaport and Eichhorn, *Arch Dermat & Syph* **49** 240 (April) 1944





into the smaller of these. Its light is reflected from a small mirror (*b*) behind it and passes through a rectangular opening (*c*) into a cavity on the top of the box (*d*), constructed to receive the test tube. Another mirror (*e*) opposite the opening (*c*) reflects the light again on the test tube. The inner walls of the smaller compartment as well as those of the test tube-receiving cavity are painted black. The box is provided with a second movable metal cover, which is connected to the outer wall of the larger compartment by means of a hinge (*f*) and which can be opened on it to the desired angle and fixed into position by means of a screw and a lever (*g*). The cover itself is made of two halves hinged in the middle so that the free half can be moved independently of the other and fixed in position by means of a screw (*h*). This free half carries a magnifier (*i*) on a sliding base, which is thus enabled to change position parallel to the long axis of the box. The magnifier itself is composed of two lenses of two different focal lengths adjustable by means of a telescopic arrangement (16 and 8 D).

Before starting his work the examiner adjusts the magnifier to suit his eyes by tilting the movable cover and sliding and extending the lenses. The test tubes can then be examined rapidly when introduced into the cavity (*d*) in a nearly horizontal position.

The larger compartment of the box is used as a container for empty test tubes and other accessories.

At this point we should like to point out a new experience in the preparation of the M-Rapid antigen. In case an antigen is too little sensitive this might be due to a low room temperature. This can be corrected by preparing the antigen in a water bath of a slightly higher temperature. For example, during winter-time we prepare our antigen in a water bath at 35 C instead of 30 C as described in the original paper. The desired sensitivity can be obtained by a variation of temperature according to circumstances.

The O-Rapid test when freshly prepared can be performed as follows. To 2 drops of serum add 1 drop of antigen, shake and centrifuge. The addition of 2 drops of isotonic solution of sodium chloride may be omitted.

Mr Edmund Katz gave technical assistance and provided designs.

### CORRECTIONS

In the article by Drs George M MacKee, Anthony C Cipollaro and Arthur Mutscheller entitled "Treatment of Tinea Capitis with Roentgen Rays" in the May issue (53:458, 1946), an excellent article on the same subject by Dr S C Shanks, which was published in the *British Journal of Dermatology and Syphilis*, August-September, 1938, was overlooked. Another good article on the subject by Drs S B Osborn, D R Tavener and F T Farmer appeared in the *British Journal of Radiology* for May 1945. This article was published too late for inclusion in the paper which appeared in the May issue of the ARCHIVES.

## Obituaries

### ROBERT CARY JAMIESON, M D 1881-1946

Dr Robert Cary Jamieson died at Harper Hospital, Detroit, on April 17, 1946 of metastatic carcinoma. He was born in Detroit on Sept 18, 1881, the son of Dr Robert A Jamieson and Emma Thompson Jamieson. He attended the Detroit public schools and graduated from the Detroit College of Medicine and Surgery in 1903. Dr Jamieson's decision to follow a medical career was no doubt influenced by his boyhood development in the atmosphere of the old style family practitioner. His father was a greatly esteemed and honored practitioner with a large practice, having started his professional career in Detroit in 1870 following his training at McGill University, Montreal, and the University of Pennsylvania.

After an internship at Harper Hospital, Dr Jamieson spent a year doing postgraduate work at the University of Vienna. He also attended clinics in London and Berlin during this period. Returning to Detroit, he became associated with Dr H R Varney, one of the early and well known Detroit dermatologists. This association lasted until 1917. He was married in 1909 to Carolyn Poppleton, who survives him.

He was appointed to the dermatologic staff of Harper Hospital in 1908 and made instructor in dermatology and syphilology at Detroit College of Medicine and Surgery. He became professor of dermatology and syphilology at Wayne University College of Medicine in 1922 and continued active in that capacity until the time of his death. He was attending physician and chief of the dermatologic service at Harper Hospital, attending physician at the City of Detroit Receiving Hospital and consulting dermatologist at Herman Kiefer Hospital.

Dr Jamieson was a member of the American Medical Association, the American Dermatological Association, the Detroit Dermatological Society and a fellow of the Academy of Dermatology and Syphilology. He was a member of the Detroit Medical Club, the Detroit Academy of Medicine and Phi Rho Sigma fraternity. He was also a member of the Detroit Athletic Club and the Bloomfield Hills Country Club.

He was active in the Wayne County Medical Society until his death. He served as secretary from 1910 to 1912, as editor of the *Detroit Medical News* from 1917 to 1918, as president from 1935 to 1936 and as trustee from 1936 to 1941. He was twice president of the Detroit Dermatological Society and served as chairman of the Section of Dermatology of the Michigan State Medical Society.

Although not a prolific writer, Dr Jamieson was the author of many publications on practical aspects of dermatologic practice

As a student and later in the early days of his practice Dr Jamieson pursued some of his boyhood hobbies, one of which, photography, continued to interest him throughout life. He was a skilled basketball player and during his earlier days played regularly in the leagues



ROBERT CARY JAMIESON, M D

1881-1946

of the Young Men's Christian Association. In later life his interest in sports found expression in his devotion to golf, in which his professional associates, with whom he constantly played, will testify that he was skilled.

Dr Jamieson had traveled widely. He took many vacation trips abroad, visiting Europe, the Mediterranean, the West Indies and South America. From these trips he brought back an impressive collection of photographs, many of which were later enlarged for exhibition purposes. Scenes in Spain, Italy and the Canadian Rockies are outstanding specimens of the amateur photographer's art. He possessed one of the finest collections of dermatologic slides in Detroit.

Modesty, honesty, kindness and good humor were outstanding traits in his character, well known to his friends and patients. He was an excellent teacher and a constant source of help and encouragement to young physicians. He possessed a combination of cordiality and dignity which, coupled with professional skill and a lively sense of humor, endeared him to his large circle of friends and patients. With a sense of irreplaceable loss and deep appreciation this tribute is tendered to the memory of a colleague and personal friend. Sympathy is extended to his family in their great loss.

L. W. SHAFFER, M.D.

## News and Comment

**American Dermatological Association**—The Sixty-Ninth Annual Meeting of the American Dermatological Association was held at the Homestead, Hot Springs, Va., on June 10 to 13, 1946.

Dr Paul A. O'Leary was elected president, Dr Charles C. Dennie, vice president, and Dr William H. Guy, director, to replace Dr C. Guy Lane, whose term had expired.

The following members were elected: Dr Herman Beerman, Philadelphia, Dr Maurice J. Costello, New York, Dr John H. Lamb, Oklahoma City, Dr Frederick G. Novy Jr., Oakland, Calif., and Dr Charles R. Rein, New York.

The meeting was attended by eighty-four members, thirty of whom read papers. The total attendance, including families of members, was one hundred and sixty.

The annual golf tournament was won by Dr J. Lamar Callaway.

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

CLINICAL OBSERVATIONS ON EARLY TRENCH FOOT CHARLES A RAGAN and ADOLPH E SCHECTER, Bull U S Army M Dept 4 434 (Oct) 1945

The authors suggest as a working hypothesis for further investigation that the following chain of events takes place in the production of trench foot Physical cold leads to vasoconstriction, which leads to anoxia Damage to the endothelial walls of the capillaries and to nerve tissue follows the anoxia The damaged nerve tissue recovers more slowly, so much so that some atrophy of the muscles results The damage to the vasoconstrictor and sweat gland-stimulating fibers is the last to be repaired

CATERPILLAR DERMATITIS SAMUEL BERKOWITZ, Bull U S Army M Dept 4 464 (Oct.) 1945

The caterpillar *Ochrogaster contraria*, its cocoon and the tail of the moth produce an acute dermatitis by local inoculation and by means of barbed hairs and of an irritating substance, the nature of which is unknown The chief manifestations of the eruption are erythematous macules which quickly progress to wheals and in fading leave many intensely pruritic papules

Treatment is palliative by means of simple antipruritic remedies Eczematogenous agents are best avoided The recognition of the eruption will prevent future outbreaks by directing a search for contaminated clothing and blankets

PEDICULOSIS PUBIS TREATMENT WITH DDT IN COLD CREAM RICHARD L SUTTON JR., Bull U S Army M Dept 4 480 (Oct) 1945

A method of treating pediculosis is submitted, with the opinion that it is efficient, harmless, cheap and free from nuisance features When the diagnosis of pediculosis pubis is established, the patient is given ½ ounce (15 Gm) of 0.5 per cent DDT (dichlorodiphenyltrichloroethane) in a cold cream base and is instructed to rub in a thin layer of this ointment under the arms, on the hairy part of the chest, about the genitalia and anus and on the hairy regions of the thighs and legs A thin layer is adequate He waits for twelve hours and then takes a bath with soap

Experience has shown that itching stops within thirty minutes, when pediculi are found to be dead, mites do not hatch, and irritation does not occur

STRAKOSCH, Denver

PENICILLIN IN NEUROSYPHILIS GEORGE D GAMMON, JOHN H STOKES, HERMAN BEERMAN, NORMAN R INGRAHAM JR, JOHN W LENTZ, HENRY G MORGAN, WILLARD STEELE and ELIZABETH KIRK ROSE, J A M A 128 653 (June 30) 1945

Sodium penicillin in solution was given intramuscularly for eight days, every three or four hours, for a total dose of 1,200,000 to 4,000,000 units to 89 patients with neurosyphilis Penicillin improved the spinal fluid in all its elements and, to a lesser degree, the serologic reactions of the blood The improvement continued for as long as four months Best results were obtained when the larger dose was given in two courses

A total dose of 4,800,000 units is recommended This may be administered as a single course or as two courses, the second given (a) at the end of the first course or (b) later, probably at the time when the results of the first have leveled off, at one hundred and twenty days

**PENICILLIN IN VINCENT'S ANGINA** BERNARD M SCHWARTZ, J A M A **128** 704 (July 7) 1945

Fourteen patients with Vincent's angina were treated satisfactorily with penicillin. The recommended dose is 100,000 units, administered intramuscularly in 20,000 unit doses every three hours.

**THE USE OF PENICILLIN IN VINCENT'S ANGINA** PAUL L SHALLENBERGER, EARL R DENNY and HAROLD L PYLF, J A M A **128** 706 (July 7) 1945

Nine patients were treated with penicillin by local application. The involved tissues were swabbed four times daily with penicillin in a concentration of from 250 to 500 units per cubic centimeter. All patients responded quickly. Two patients were treated with penicillin alone, administered intramuscularly, the recommended dosage is 15,000 units every three hours for eight doses. The duration of hospitalization was reduced by penicillin therapy below that needed for treatment with sulfadiazine lozenges, hydrogen peroxide and sodium perborate, chromium trioxide and silver nitrate and o-phenarsine hydrochloride.

**WAR AND DERMATOPHYTOSIS** FRED D WEIDMAN, CHESTER W EMMONS, JOSEPH HOPKINS and GEORGE M LEWIS, J A M A **128** 805 (July 14) 1945

Ointment of benzoic and salicylic acid and boric acid powder compare well with sodium propionate and cresatin-Sulzberger (metacresyl acetate) as fungicides. Although fungi cause the majority of intertrigos of the toes, bacteria and sensitization are responsible for a considerable number. Repetition of attacks of dermatophytosis usually represent recurrences. Foot baths (sodium hypochlorite and sodium thiosulfate) are of negligible prophylactic value. Dermatophytosis does not predispose to contact dermatitis. In treatment, sodium propionate, undecylenic acid and cresatin-Sulzberger have emerged as useful fungicides.

**PENICILLIN AND SULFONAMIDES IN THE THERAPY OF ACTINOMYCOSIS** LEONARD DOBSON and WINDSOR C CUTTING, J A M A **128** 856 (July 21) 1945

Sulfonamide compounds and penicillin are highly effective drugs in the treatment of actinomycosis. Of 16 patients treated with sulfonamide compounds or penicillin 7 were cured, in 7 the disease was arrested, while 2 died. In vitro tests corroborate the clinical impression of the varying susceptibility of different strains of Actinomyces to sulfadiazine and penicillin. Unless exceptionally high concentrations are used, penicillin appears to be slightly inferior to sulfadiazine against this fungus. The combination of the two drugs in usual dosage does not improve the results.

**CALLUSES, CICATRICES AND OTHER STIGMAS AS AN AID TO PERSONAL IDENTIFICATION** FRANCESCO RONCHESI, J A M A **128** 925 (July 28) 1945

In event of unobtainable fingerprints, in amnesia, and in other instances stigmas of disease or occupation may be a valuable aid for personal identification. Schwartz, in the discussion of Ronchese's article, classified industrial stigmas as results of (1) physical forces, such as heat, cold and radiation, (2) mechanical causes, such as pressure and friction, and (3) chemical causes.

Club nails, Beau's lines and spoon nails are interesting observations, but of no diagnostic value.

**DERMATOSES OF THE HANDS** C GUY LANE, ETHEL M ROCKWOOD, CARL S SAWYER and IRVIN H BLANK, J A M A **128** 987 (Aug 4) 1945

Many of the cutaneous disturbances of the hands which are now referred to as dermatomycosis, dermatophytid contact dermatitis, housewives' eczema, dermatitis due to soap, neurodermatitis, nummular eczema or bacterid should be more correctly

called "infectious eczematoid dermatitis." An eruption of the hands may develop from any of a number of causes, it may be a true contact dermatitis, dermatomycosis, dermatophytid or other dermatosis, or the skin may suffer mechanical or thermal trauma. Any one of these cutaneous disturbances, together with one or more of the following factors—excessive use of soap and water, vasomotor instability, trauma, menstruation, hot or cold weather, the presence of an infection in some other organ or tissue—alters the relationship between the host and the normal resident flora of the patient's skin. Micro-organisms of the resident flora, probably of low virulence, invade the skin. Subsequently a sensitization to some bacterial decomposition product may develop. From this point, the eruption progresses primarily because of the invasion of the bacteria, and even if the causal agent of the original cutaneous disturbance is withdrawn the eruption persists and perhaps extends or even changes its character. Direct invasion of the hands or feet by a filamentous fungus, the use of soap and water, and contact with a specific allergen are less frequent causes of dermatitis of the hands than is now generally supposed. Four hundred and seventy-five cases of "eczematoid" dermatoses of the hands were studied. Initial therapy consisted of soaking the hands in solution of boric acid or application of compresses during the acute phase and use of a mild lubricating ointment, such as boric acid ointment or paste of zinc oxide, during the dry fissured desquamating phase. A soapless regimen is recommended.

CARCINOMA OF THE ORAL CAVITY. EDWIN A. LAWRENCE and PHILIP S. BREZINA, J. A. M. A. **128** 1012 (Aug. 4) 1945

Of 145 consecutive cases of carcinoma of the oral cavity, the best results were in the groups in which the buccal mucous membranes and anterior parts of the tongue were involved, in which a five year survival rate of 23 per cent was obtained. The poorest result was in the group with hypopharyngeal lesions, in which the five year survival rate was 8 per cent.

If epidermoid carcinoma is to be destroyed, a dose of at least 5,000 r must be delivered into the tumor. This usually requires supplementary interstitial administration of radon in addition to roentgenotherapy. The roentgen radiation should be administered for approximately twenty-one treatment days, and radon seeds should be inserted when the tumor has regressed to its maximum degree.

There is a possible relationship of the prolonged presence of oral infection and carcinoma of the mouth, pharynx and upper part of the gastrointestinal tract. The treatment of carcinoma in the mouth and pharynx is essentially a radiologic problem, since in only a small number of cases are the tumors suitable for surgical removal. To treat metastatic disease successfully, a radical neck dissection must be done early.

LOEFFLER'S SYNDROME ASSOCIATED WITH CREEPING ERUPTION (CUTANEOUS HELMINTHIASIS). D. O. WRIGHT and EDWIN M. GOLD, J. A. M. A. **128** 1082 (Aug. 11) 1945

Twenty-six cases of creeping eruption with classic cutaneous manifestations were studied. Fifteen of the cases were observed for a period of two weeks or more. In 9 of the 15 cases transient migratory pulmonary infiltration, peripheral eosinophilia and paucity of clinical signs or symptoms of systemic disease were demonstrated, fulfilling the criteria of Loeffler's syndrome.

THE TREATMENT OF IMPETIGO CONTAGIOSA WITH SULFATHIAZOLE IN AN ALCOHOLIC PLASTIC VEHICLE. R. H. DRAEGER and MICHEL PIJOAN, J. A. M. A. **128** 1096 (Aug. 11) 1945

Sulfathiazole in an alcoholic plastic jelly is highly effective in the treatment of impetigo contagiosa. It obviates the necessity for bandaging the lesions. The plastic film limits the spread of infection. The presence of exudate liberates the sulfathiazole from the water-soluble film at the proper site.



DISSEMINATED CONGENITAL OSTEOMAS OF THE SKIN WITH SUBSEQUENT DEVELOPMENT OF MYOSITIS OSSIFICANS FRANK VERO, GERALD F MACHACEK and FREDERIC H BARTLETT, J A M A **129** 728 (Nov 10) 1945

The authors report a case of disseminated osteomas of the skin in an infant. The lesions were seen immediately after birth on the scrotum and the trunk. They were most numerous on the left lower extremity. When the child was 2 years and 11 months old, a diagnosis of myositis ossificans progressiva was made because of the development of hard masses in the left popliteal region and on the left buttock. They were deeply seated and involved the musculature.

Many cases reported in the literature as ones of true osteomas have not been accepted as such. Secondary ossifications following various pathologic processes of the skin are more frequent and are presumed to be metaplastic. The diagnosis of true osteoma may be accepted when it occurs early in life or when found in nevi and when not preceded by other pathologic changes in the skin. True, or primary, osteomas are believed to develop from dispersed embryonal cells. The clinical diagnosis of osteoma of the skin is usually established only after biopsy and subsequent microscopic examination. Roentgenograms may be of aid in the diagnosis, as they show opaque shadows or structureless densities, thus detecting lesions which escape inspection and palpation.

EPIDERMOLYSIS BULLOSA IN THE NEWBORN ROBERT A BLACK, EMMANUEL WILHELM, CHARLES S GILBERT and CLEVELAND J WHITE, J A M A **129** 734 (Nov 10) 1945

In the simple form of epidermolysis bullosa of the newborn the bullae appear on the skin after mechanical irritation or slight trauma. The disease is usually congenital, the lesions may be present at birth or may appear first from a few days to two or three years after birth. The mucous membranes are not affected, and the nails are not involved. The blebs heal without leaving scars, and there is no permanent alteration of the skin.

In the dystrophic form the hereditary nature of the disease is present but is not so pronounced as in the simple form. The bullae appear at or soon after birth, as in the simple form, and arise after trauma. They are most likely to become hemorrhagic. In healing, crusts and scabs are formed, resulting in permanent pigmentation and scarring. Extensive degeneration of the nails is a constant characteristic of this type. The buccal mucosa and the tongue show bullae, ulceration and leukoplakia, and there may be scarring of the lips.

Practically all investigators believe that the bullae may be ascribed to a modified susceptibility or reactivity of the skin to injury, or to an increased irritability of the integument, which under normal conditions would result only in transient hyperemia. There is more or less constant reduction and degeneration of the elastic tissue of the skin.

The authors report a case which belongs to the small group described by Herlitz as "epidermolysis bullosa hereditaria letalis." Bullae were present on two fingers at birth. Subsequent involvement of the whole integument and mucous membrane of the mouth, tongue and pharynx occurred. Secondary infection and constitutional debilitation resulted in early death. The mother had had two previous babies who died soon after birth, each having had a blister-like eruption.

HENSCHEL, Denver

SULPHANILAMIDE DETERMINATION IN SPONTANEOUS AND CANTHARIDIN BLISTERS IN VESICULAR AFFECTIONS OF THE SKIN (PEMPHIGUS, DERMATITIS HERPETIFORMIS, HERPES GESTATIONIS, EPIDERMOLYSIS BULLOSA HEREDITARIA) A DOSTROVSKY and F SAGHER, Brit J Dermat **57** 85 (May-June) 1945

After treatment with various sulfonamide compounds 15 persons were examined for the presence of the drug in "blisters" of the skin. Of these, 7 had lesions of the pemphigus type, 7 were controls, whose "blisters" were spontaneous as well

as artificially produced by cantharidin and 1 had "blisters" caused by potassium iodide. In all the presence of a sulfonamide compound in the contents of the "blisters" could be established. A certain interdependence was noted between the "blister" level and that of the blood. Sulfonamide drugs penetrate into established "blisters" and gradually disappear from them after administration of the drug is stopped. This indicates the simple mechanism of diffusion of the substance, no matter whether the "blisters" are still growing through an increase of fluid or are about to disappear. Twelve hours after the last dose had been given, the level established in the contents of the "blisters" was, as a rule, higher than that of the blood. Determination of the "blister" level may, therefore, replace analysis of the blood when the presence of a drug in the blood is sought.

BLUFFARD, Chicago

TREATMENT OF HUMAN CUTANEOUS ANTHRAX WITH PENICILLIN H. STOTT,  
Brit M J 2 120 (July 28) 1945

A 70 year old man with a lesion on the left jaw from which anthrax bacilli were recovered was treated with a total of 200,000 units of penicillin. The clinical response was remarkable.

SORE FINGER-TIPS IN INDUSTRY. PROTECTION BY HYDROGEN PEROXIDE J. VINCENT  
BATES, Brit M J 2 154 (Aug 4) 1945

An accidental observation by the operator of a wire-stitching machine in a paper bag factory led to the discovery of a method which largely protects the skin of the finger tips from damage by the constant friction in this work. The operators are instructed to dip the finger tips into a bottle containing 20 volume hydrogen peroxide. The number of applications necessary to afford protection varies from three times a week to four times a day.

A SUBSTITUTE FOR UNNA'S PASTE J. J. WILD, Brit M J 1 409 (March 24) 1945

Wild describes a substitute for Unna's paste. The basis is methyl cellulose, a water-soluble substitute for tragacanth. To prepare the substitute take 95 parts of water and 5 parts of methyl cellulose, leave over night, stir thoroughly and then adjust the proportion to 3 per cent with water. Add 20 per cent zinc oxide and stir well.

Since this preparation is not antiseptic, it must be freshly prepared for use. It is applied cold to a wet bandage with a brush and layers of wet bandage are impregnated with it in the same way as with Unna's paste.

CAROTINAEMIA IN THE TROPICS E. COCHRANE, Brit M J 1 483 (April 7) 1945

The author reports a case of carotenemia in which the patient's diet included 3 to 5 pounds (1.3 to 2.3 Kg) of papaw daily. An examination of the serum showed an increase of lipochromes.

PENICILLIN REACTION W. MICHIE and S. W. C. BAILIE, Brit M J 1 554  
(April 21) 1945

Sensitization to penicillin following the local application of the drug is described. The result of a patch test with penicillin was strongly positive. It was impossible to determine whether the causative factor was the penicillin itself or impurities in it.

POLYNEURITIS AFTER JUNGLE SORES R. L. WARD and A. S. MASON, Brit M J 2 252 (Aug 25) 1945

During military operations in Burma many men had multiple indolent ulcers of the extremities, commonly known as "jungle sores". It was noticed that in

several of those there later developed a peripheral neuritis. Twenty-one cases were observed, in all of which the disease followed a constant pattern. A prominent feature was the loss of accommodation in 16 out of the 21 cases. After careful study, it was concluded that the cause was toxins of diphtheritic origin. Disability lasted from six months to one year. None of the affected persons had been immunized against diphtheria or had previously suffered from the disease.

SCABIES AND D D T F F HELLIER, *Brit M J* 2 255 (Aug 25) 1945

The success of DDT (dichlorodiphenyltrichloroethane) in preventing infestation by lice has caused wonder as to whether it has any effect on scabies. To determine whether DDT had any prophylactic action against scabies, the author examined a series of infested soldiers to see how many had been wearing clothing impregnated with DDT or had been using the powder regularly within two months prior to the onset of scabies. The almost exact agreement of results for the patients with scabies and those for the controls showed that DDT has no preventive action against the acquiring of scabies.

ERYTHEMA NODOSUM AND TUBERCULOSIS WILLIAM D GRAY, *Brit M J* 2 286 (Sept 1) 1945

Nine cases of erythema nodosum are described, in 7 of which the patients gave a history of definite or possible contact with tuberculosis. All the children had positive tuberculin reactions, and none gave a history of rheumatism.

The author feels that erythema nodosum is often associated with tuberculous lesions and is a manifestation of tuberculous infection. He recommends that every case of erythema nodosum should be regarded as a newly infected case of tuberculosis and therefore search be made among contacts for the source of infection.

FIRST-AID TREATMENT OF PHOSPHORUS BURNS W McCARTAN and E FECITT, *Brit M J* 2 316 (Sept 8) 1945

The ease with which copper combines with active phosphorus to form copper phosphide has been the basis of most methods of first-aid treatment of persons contaminated with phosphorus. A new treatment, the use of a copper-soap compound, has been found to be a more effective treatment than the standard methods, and, in addition, being viscous and compact, the substance can be carried about easily by nurses, fire guards and others. For convenience in handling, the compound was made in lots of  $\frac{1}{2}$  pound (225 Gm). It is prepared as follows: A 25 per cent solution of copper sulfate in water was prepared, and the requisite amount of this to give a final content of 4 per cent copper salt was heated in a boiling flask. Medicinal soft soap was heated in a water bath, and the copper sulfate solution was added hot by constant trituration on a slab. Copper precipitates as the oleate, and this is thoroughly incorporated into the base between each addition. It is advisable to add the copper sulfate solution in small successive portions. The resulting compound is a tacky homogeneous mass, samples of which have kept well for at least twelve months.

THE ROLE OF ANIMAL-TYPE DERMATOPHYTES IN HUMAN RINGWORM BERNARD A THOMAS, MARY LENNOX and J T DUNCAN, *Brit M J* 2 346 (Sept 15) 1945

An account is given of an outbreak of dermatophytosis in which 5 persons directly and 4 persons indirectly were infected from a puppy. The authors emphasize the value of cultural investigation, and stress is laid on the importance and practicability of treating by conservative methods ringworm of the scalp produced by fungi of animal type.

## CUTANEOUS SCHISTOSOMIASIS K O BLACK, Brit M J 2 453 (Oct 6) 1945

In a series of 130 cases of schistosomiasis in Europeans, the patients in 4 cases were seen with distinctive cutaneous lesions described as deep, shotty, pink papules 3 to 5 mm in diameter, arranged singly or in clusters. An area of erythema develops around each papule, and these areas become confluent. Papules remain for about six weeks or more changing to a dull red or purplish color and some become softer with a white spot at the apex, the contents of which are white and pasty. Tissue juice aspirated from the cutaneous nodules contained eggs of *Schistosoma haematobium* identical with those seen in the urine and feces.

SHAW, Chattanooga, Tenn

## CUTIS VERTICIS GYRATA (TYPE NEURO-NAEVUS) H JARGER, Dermatologica 86 253 (Oct-Nov) 1942

A 54 year old man has had since infancy a slowly growing malformation of the scalp. On the crown and the occipital and the right temporal regions a caplike growth with pads and furrows, similar to cerebral convolutions, has formed. It is more or less sharply limited and of soft consistency with some firm nodules. Its surface looks like normal but coarse skin. It is grayish and has dilated pores and sparse hair. It is freely movable over the skull. The roentgenogram shows a normal sella turcica and mild occipital hyperostosis.

With Masson's and Van Gieson's stains one sees in the considerably thickened deep layers the collagenous tissue replaced by numerous neuroid plexiform bundles, which extend vertically or obliquely toward the surface and form tortuous laminae with fibers and a multinuclear syncytium. Its irregular spaces are filled with cells of the type of nevus cells which in the upper layers of the corium either are arranged in bands or small groups or are isolated. The epidermis and the appendages are without changes. Some perifollicular and perivascular infiltration with lymphocytes and histiocytes is present. The histologic diagnosis is neuro-nevus of Masson of the scalp. This case is similar to the one described by Lenormant in 1920. The location in the area of the fontanels where malformations are frequent is no accident. The disturbance must have interfered with the development of the embryonic ectoderm, which forms the tissue of the skin and the nervous system.

In the discussion Lutz remarks that cases corresponding to Jadassohn's and Unna's original description of cutis verticis gyrata look quite different. In cases of cutis verticis gyrata the almost normal integument of the scalp can be lifted up in folds, as if the skin has become too loose. In the case under discussion a tumorous growth consisting of increased tissue and tumor cells extends far beyond the level of the normal skin. He suggests the term "naevus cerebriformis".

HELEN O CURTH, New York

## DEEP CUTANEOUS MONILIASIS A FATAL CASE OF A PECULIAR TYPE N DANBOLT, Acta dermat-venereol 21 98 (Feb) 1940

A man 78 years old appeared with localized lesions over both supraorbital ridges. They were erythematous, infiltrated, about 3 cm in diameter and depressed in the center. The margin of the lesions presented numerous small abscesses. The leukocyte count was 172,000. The sedimentation rate was 129 mm. In a few weeks the lesions became much larger, and a new lesion appeared in the occipital region. The patient was then hospitalized. Within eight days after his admission, infiltrated lesions appeared on the cheeks and scalp. These progressed and became depressed in the center, and pustules developed around the edges. With further progression the lesions covered the entire face. The general health of the patient was good except for a hyperglycemia without glycosuria. After three weeks of hospitalization bullae appeared on the extremities. These bullae then discharged their contents, which were tinged with blood, leaving the floor of the lesions covered with papillomatous masses. The neighboring epidermis loosened, and the process

spread peripherally and finally covered the neck, chest, axillas, arms and legs. The patient became febrile and died within four months after the appearance of the initial lesions.

Complete bacteriologic studies revealed the presence of *Monilia stellatoidea* in pure culture. In microscopic sections and in smears of the exuding pus the organism could be detected in large amounts. In the histologic examinations, granulation tissue rich in cellular elements was seen penetrating down into the subcutaneous tissue. The cells consisted of neutrophilic granulocytes, fibroblasts, some lymphocytes and plasma cells. On postmortem examination the only positive finding other than the cutaneous lesions was the presence of bronchopneumonia on the left side.

Treatment was attempted with potassium iodide, sulfonamide compounds and insulin, without any benefit. One of the reasons that a species of *Monilia* caused such a rapidly progressing fatal infection of the skin is assumed to depend on the increased disposition of the tissues due to the hyperglycemia.

FURTHER EXPERIMENTS ON SENSITIZATION OF THE SKIN WITH DINITROCHLOROBENZENE H. HAAHNSHAUSEN, *Acta dermat-venereol* **21** 158 (Feb) 1940

Sensitization of the corium as well as the epidermis was caused by the use of 2,4-dinitrochlorobenzene in topical application and through intracutaneous injection. It is also possible to sensitize the previously normal skin by subcutaneous injections, but this method requires the use of larger doses. All attempts to produce hypersensitivity through intramuscular injections failed when a solution of the pure drug was used.

When dinitrochlorobenzene was mixed with horse serum it had the same sensitizing effect by intracutaneous injection as the solution of the pure drug, but it was also possible with the use of larger doses to sensitize the skin by the use of intramuscular injections. Foreign protein was not necessary in the latter method, because a mixture of dinitrochlorobenzene and the patient's own serum produced the same results as the mixture of the drug and horse serum. This seems to indicate that the effect is caused by a linkage of the dinitrochlorobenzene to the protein of the serum.

ROBINSON, Washington, D. C.

# Society Transactions

## HAWAII DERMATOLOGICAL SOCIETY

James T. Wayson, M.D., *President* †

Harry L. Arnold Jr., M.D., *Secretary*

*March 10, 1945*

### A Case for Diagnosis (Deep Fungous Infection?) Presented by DR. HARRY L. ARNOLD, JR., Honolulu, Hawaii

K. M., a 27 year old Japanese laborer, was first seen on Dec. 30, 1944, because of a group of lesions about the left knee, present and spreading slowly since he received a cane knife cut there at the age of 10.

Examination disclosed multiple irregular depressed atrophic scars about the left knee and several rubbery hard, subcutaneous masses, 2 to 5 cm. in diameter, above the knee. There was no redness or tenderness. There was one shallow crusted ulcer, 3 mm. in diameter.

The hemogram was normal. The urine was normal. Serologic tests for syphilis (Kolmer-Wassermann and Eagle) elicited negative reactions on two occasions. Roentgenograms of the knees showed no bony abnormality. Pus obtained on two occasions, by deep aspiration of one of the masses and by opening a superficial pustule, gave no growth on Sabouraud's medium (both at room temperature and at 37° C), chocolate agar and Brewer's aerobic-anaerobic medium, after four weeks.

Biopsy of one of the rubbery subcutaneous masses showed extensive deep-seated, chronic suppurative inflammation, with multiple abscesses surrounded by a banal admixture of neutrophils, histiocytes, fibroblasts, lymphocytes and plasma cells. Considerable hemosiderin was present. Gram stains revealed no organisms.

A week's administration of the usual doses of sulfadiazine, with a blood level of 10.6 mg. per hundred cubic centimeters, produced no change in the lesions.

#### DISCUSSION

MAJOR TIBOR BENEDEK, M.C., A.U.S. (by invitation) What is the situation in Hawaii with respect to sporotrichosis?

DR. HAROLD M. JOHNSON I see 2 or 3 cases a year, all of the localized lymphangitic type.

MAJOR TIBOR BENEFER, M.C., A.U.S. (by invitation) I should suggest repeating the cultures, because sometimes *Sporotrichum* is difficult to identify both in histologic sections and in cultures. I should refer you to "Les sporotrichoses," by De Beurmann and Gougerot, published in 1912. There are mentioned there, and I can recall in my own experience, clinical pictures somewhat like this and, like this, of long duration. The *Sporotrichum* in histologic sections is reduced to tiny, yeastlike cells which may be difficult to identify. I would suggest repeating the cultures on Sabouraud's medium at room temperature. The case presented is not at all the picture of blastomycosis, it is too deep seated and not destructive enough.

LIEUTENANT COLONEL CARL F. TRUSSMER, M.C., A.U.S. (by invitation) I obtained the history from the patient that at a time when the lesion was draining the pus contained granular material.

DR. HARRY L. ARNOLD JR. We found one such granule and examined it in the laboratory, but it was entirely amorphous.

† Dr. Wayson died Jan. 17, 1945.

LIEUTENANT COLONEL CARL F TESSMER, M C, A U S (by invitation) I don't see why it couldn't be actinomycosis, with these occasionally draining sinuses

DR. HARRY L ARNOLD JR I think the absence of any bone involvement after seventeen years is against that diagnosis

MAJOR TIBOR BENEDEK, M C, A U S (by invitation) I agree that this makes it extremely unlikely

DR HAROLD M JOHNSON This does not impress me as an example of sporotrichosis

MAJOR TIBOR BENEDEK, M C, A U S (by invitation) The localized form of this disease is unusual but not rare De Beurmann and Gougerot, in Southern France, reviewed many such cases Some had been diagnosed tuberculosis and in at least half of those cases there had been amputations of arms or legs Of course, there were those more fortunate patients who were given the mistaken diagnosis of syphilis These were given iodides, and promptly got well It behaves much like syphilis in that respect—iodides are specific

#### **Dermatitis Herpetiformis Occurring in Twins** Presented by MAJOR GERARD A DE OREO, M C, A U S

Twins of Austrian-Jewish ancestry, aged 25, were referred to the hospital because of a chronic pruritic dermatosis of twenty-six months' duration They had been assigned to organizations separated by many miles About November 1942, when seeing each other for the first time in three months, each noted that the other had an eruption similar to his own This did not surprise them, for throughout their lives they had suffered from the same maladies simultaneously They had had measles, mumps, chickenpox and lobar pneumonia together

Examination of the skin of each shows essentially the same findings A generalized, grouped and symmetric papulovesicular eruption involving the wrists, arms, sacral area, buttocks, groin, thighs, legs, ankles and dorsa of the feet In addition to the active lesions there are many small hyperpigmented macules and a few scars marking the sites of former lesions The scalp, mucous membranes and genitalia are free from lesions

The reactions to serologic tests for syphilis were negative, and the urinalysis and hemogram were normal Repeated blood studies disclosed an eosinophilia in each patient varying from 1 to 3 per cent

Patch tests with 50 per cent potassium iodide were performed on the ankle of each patient, giving rise to an acute erythematopapulovesicular reaction after twenty-four hours One twin was given 10 minims (0.6 cc) of saturated solution of potassium iodide orally three times daily, there was an exacerbation of all existing lesions and development of new papules after four days During this time the pruritus increased, and the patient complained of pain and burning This patient has received sulfapyridine, 3 Gm daily, and a low salt diet for but one day at the time of this presentation

Histologic examination of the skin of the other twin revealed several intradermal and subepidermal vesicles The papillary portion showed signs of acute inflammation with some vascular and perivascular infiltration There were numerous eosinophils in both the vesicles and the surrounding tissue

#### DISCUSSION

DR HARRY L ARNOLD JR Isn't this a unique occurrence?

MAJOR GERARD A DE OREO, M C, A U S These two brothers were presented not because the disease entity is so unusual, but rather because the appearance of dermatitis herpetiformis in twins has not been recorded to my knowledge Certainly the appearance of this uncommon dermatosis simultaneously in twins who have lived apart would invite speculation that Dühring's disease may be the result of some constitutional abnormality, a possible ectodermal defect, rather than an infectious process as some investigators have suggested

**Hyperkeratosis Follicularis et Parafollicularis in Cutem Penetrans**  
(Kyrle's Disease) Presented by MAJOR TIBOR BENEDEK, MC, AUS  
(by invitation) and MAJOR GERARD A. DE ORO, MC, AUS

A 27 year old Negro soldier, who had been in the service one year, was admitted to the hospital because of an erythematous squamous eruption of the genito-crural region

Examination shows a tender spot in the center of the left sole. This has become increasingly tender and painful to even the slightest pressure, and has impeded the patient in walking. The lesion is mound shaped and papular, 12 by 14 mm in diameter and 2 mm high, with a crater 2 mm in diameter at the mouth, depressed in a funnel shape 2 mm below the skin surface and filled with hyperkeratotic detritus.

There is a similar lesion in the center of the mesial edge of the right side. This lesion is not constantly painful because it is not exposed to heavier or constant pressure. It is a flat papule about 5 mm in diameter, with a central crater also filled with hyperkeratotic material. This lesion is in an earlier stage of development than that on the left sole.

There are similar lesions around the ankles and on the legs. One is about 12 cm above the right external malleolus, on the anterolateral surface of the right leg. It is also a flat papule 3 by 5 mm in diameter, with a central crater about 2 mm in diameter, filled with hyperkeratotic material, and due to its location not yet painful. Another lesion, early and typical in form and developmental stage, is located exactly over the right achilles tendon about 10 cm above the heel. It is 1.5 to 2 mm broad, round, with a shallow, cuplike depression 1 mm deep in the center and with a conspicuous elevated rim. One can compare these early lesions with depressions caused by the pressure of the tip of a blunt pencil into the surface of the skin. Their sudden appearance and cuplike shape are even more comparable with similar depressions developing on the surface of a Petri dish agar culture of *Bacillus coli*, for instance, and caused by the sudden appearance of phages.

A new lesion has appeared about 10 mm below the tip of the right thumb on its volar surface, and a similar lesion on the plantar surface of the left big toe almost in its center. The cup-shaped depressions in these would take up the round head of a pin at present.

Biopsy of two lesions on the right leg and the left sole showed a huge keratinous plug which displaced the epidermis abruptly downward, penetrating into the corium, and stretching the epidermis very thin across the rounded innermost portion of the plug.

The urine was normal. The Kahn reaction of the blood was negative. The hemogram was normal.

#### DISCUSSION

MAJOR TIBOR BENEDEK, MC, AUS (by invitation) This disease was first described by Kyrle in 1916. Since that time, a total of only 8 or 10 cases have been reported, all in the German and Danish literature. The name of this disease is not only admirably descriptive but it is also exhaustive. The histologic picture is unique. I have previously seen 1 example of this disease, also in a Negro soldier. One of his lesions had been destroyed by desiccation but had recurred. I thought it had not been completely destroyed, so I repeated the operation, and it recurred again. I then excised the lesion widely and it recurred once more. It was necessary to discharge the man from the service because of the disability produced by the pain of this lesion.

DR. HARRY L. ARNOLD, JR. The histologic picture is perhaps closer to that of *clavus* than anything else, but still it is not by any means the same.

MAJOR TIBOR BENEDEK, MC, AUS (by invitation) No, it is not. It is almost as if the epidermis were a rubber band, fixed at two points, with pressure applied to it from one side until it actually breaks under the pressure.



**Pityriasis Lichenoides et Varioliformis Acuta** Presented by DR HARRY L. ARNOLD JR

L. E., a 23 year old mechanic of Caucasian ancestry, was first seen Jan 10, 1945, because of a generalized and moderately pruritic eruption of two weeks' duration

The eruption is generalized, but much more profuse on the trunk and mesial aspects of the arms than elsewhere, no lesions are seen on the palms, the soles, the genitalia, the face or the mucous membranes. The eruption consists of discrete, oval, brightly erythematous, shotty papules from 2 to 6 mm in diameter, a few are bluish and some are capped by thin crusts

Red and white blood cell counts were within normal limits, there was no neutropenia or eosinophilia, the urine had a  $pH$  of 7 and contained albumin (4 plus) and red blood cells (1 plus), serologic tests for syphilis (Kolmer-Wassermann and Eagle tests) elicited negative reactions

Biopsy showed a sharply defined papule formed by a dense polymorphous cellular infiltrate, with simple necrosis of the epidermis immediately overlying it. A few patches of the infiltrate, which like the main portion consisted of lymphocytes and plasma cells with an admixture of a few fibroblasts or histiocytes, neutrophils, and eosinophils, were present deeper in the corium

The patient was given weekly intramuscular injections of 0.2 Gm of bismarsen. At the fourth visit it was apparent that the eruption was fading rapidly, at the sixth a new crop of lesions was beginning to appear, but they were small and sparse, and at the end of a week they were already visibly subsiding. The eighth injection was given on March 5

## DISCUSSION

The members agreed with the diagnosis as presented

**Fox-Fordyce Disease Two Cases** Presented by DR HARRY L. ARNOLD JR

K. K., a 17 year old Japanese girl, was first seen Feb 17, 1945, because of a pruritic folliculitis of the axillas and pubic region of six months' duration. She was hospitalized with a tentative diagnosis of sycosis, and treated with continuous wet packs, using 100 units of penicillin per cubic centimeter of isotonic solution of sodium chloride. The crusting and secondary inflammatory reaction disappeared rapidly under this regimen, but the itching was not relieved at all

Examination after healing of the secondary folliculitis shows a profuse eruption of discrete, light brown, barely elevated follicular papules throughout the hairy portions of both axillas and on both labia majora

The surrounding skin was shielded with lead rubber, and the hairy portions of both axillas were given 400 r of roentgen rays filtered through 0.5 mm of aluminum, using a peak of 80 kilovolts, 5 milliamperes, with the anode 30 cm from the skin, and for an exposure of eight hundred seconds. The half value layer by this technic is 1.5 mm of aluminum, the epilating dose roughly 380 r and the erythema dose roughly 420 r

S. S., a 26 year old unmarried Japanese woman, was first seen March 5, 1945, because of an intensely itchy dermatosis present in the axillas about seven months, in the genital region about three months and about the nipples for only a few weeks

Examination disclosed a healthy-looking young Japanese woman with a profuse eruption of discrete brown follicular papules throughout the hairy portions of both axillas, on the labia majora and, to a much less extent, about both nipples, on the areolas

The skin surrounding the involved portion of the left axilla was shielded with lead rubber and the area was given 400 r of roentgen rays filtered through 2 mm of aluminum, using a peak of 80 kilovolts, 5 milliamperes, with the anode 30 cm from the skin and for an exposure of one thousand six hundred seconds. The half value layer by this technic (determined by extrapolation) is roughly

6 mm of aluminum, the epilating dose roughly 380 r and the erythema dose roughly 500 r

NOTE—Neither patient had any relief from pruritus three weeks after the treatment

## DISCUSSION

DR HARRY L. ARNOLD JR I recently reported in the "Proceedings" of the Staff Meetings of The Clinic, Honolulu, a case of Fox-Fordyce disease, repeatedly irradiated with only temporary success, in which the administration of solution of potassium arsenite, U S P, was promptly followed by disappearance of both the itching and the lesions. The patient has remained well for nearly five years

### Scleroderma, Circumscribed Presented by CAPTAIN HERBERT LAWRENCE, MC, AUS

A 31 year old American Red Cross worker, Caucasian, stated that about ten years ago she first noticed a whitish discoloration of the skin on the volar aspect of the right forearm. The lesion spread up and down the forearm, and soon thereafter similar lesions appeared in the flexure of the left elbow and on the right shoulder. About three years ago another lesion appeared on the right cheek. One year ago another area of involvement appeared over the dorsum of the left hand at the base of the thumb. The patient received her most recent dermatologic treatment about three years ago in Washington, D C, it consisted of administration of thiamine hydrochloride and sulfonamide drugs over a period of about six months, interrupted by a one month period of rest. The patient stated that her hands and feet were excessively cold and uncomfortable in cold climates. The fingers become flushed when exposed to cold air and she has noticed a tingling sensation in her legs extending from the thighs to the feet, this sensation becomes intensified on exercise and is relieved by rest.

Examination shows brownish white mottling of the skin of the face, particularly on the right side and extending to the neck. Extending over the lower part of the neck and onto the upper portion of the chest there are linear striae which are composed of hypertrophic glandular orifices. In the right clavicular region there is a large hyperpigmented patch with definite atrophy, in which numerous telangiectases can be seen. On the volar aspect of the right arm, extending from the wrist to just above the elbow flexure, there is a striated area of hyperpigmentation and hypopigmentation which the patient states originally appeared as a whitish patch and then gradually became brownish purple in color, with the adjacent areas following that same cycle and becoming so affected. Near the base of the left thumb there is a dollar-sized patch, a portion of which is hypopigmented and suggests scleroderma to the touch, while the remaining portion of the area does not present the feel of scleroderma and is hyperpigmented.

## DISCUSSION

MAJOR GERARD A. DE ORO, MC, AUS The skin on most of the patient's lesions was not at all hidebound, but was soft, pliable and slightly hyperpigmented. A large plaque on the right clavicular area showed considerable telangiectasia which suggested poikiloderma.

DR HARRY L. ARNOLD JR That was my diagnosis, also. The skin was not at all bound down, except for the lesion on the left thumb.

DR HAROLD M. JOHNSON I think that the patient has multiple lesions of localized scleroderma, which have for the most part healed. The patch on the left thumb still is typical morphea.

MAJOR TIBOR BENEDEK, MC, AUS (by invitation) I think that it is definitely a healed morphea. The active patch on the left thumb leaves no doubt of that diagnosis, in my opinion.

CAPTAIN HERBERT LAWRENCE, MC, AUS She has some symptoms of Raynaud's disease from time to time, too.

DR HAROLD M JOHNSON Yes, and because of that she should stay in Hawaii, if possible, and not return to a cold climate Her prognosis here should be relatively good

**Herpes Gestationis** Presented by DR HAROLD M JOHNSON

M G, a 24 year old Caucasian woman, had a severe pruritic dermatitis of the legs, the thighs and the abdomen in the fourth month of pregnancy During the latter part of a previous pregnancy she had had "urticaria"

Since the fifth month of the present pregnancy she has had itching around the umbilicus followed by small "urticarial" papules on the legs The lesions are increasing, and there are large plaques of weeping, crusted lesions on the ankles and the thighs The itching and burning are almost unbearable During the last month new lesions have been appearing on the thighs and the arms with polymorphic configuration varying from small, circinate lesions the size of a quarter to larger polycyclic plaques Large vesiculobullous lesions periodically appear on the ankles, the thighs and the abdomen

Various antipruritic preparations gave no relief from itching and burning Colloid baths tended to irritate her skin Sulfapyridine, 60 grains (3.9 Gm) daily, gave relief promptly, but relapse occurred after a week

Examination of fluid from bullous lesions showed 6 per cent eosinophils

The blood count showed 60 per cent hemoglobin, 3,840,000 red cells, 16,800 white cells, polymorphonuclear neutrophilic leukocytes, 66 per cent, lymphocytes, 22 per cent, and eosinophils, 11 per cent The urine was normal Wassermann and Kahn reactions of the blood were negative

DISCUSSION

DR HAROLD M JOHNSON According to Costello, most of these cases of herpes gestationis have their onset in the vicinity of the umbilicus

DR HARRY L ARNOLD JR I have certainly found that to be the case with urticaria in pregnant women I have frequently seen it begin in the abdominal striae

MAJOR TIBOR BENEDEK, MC, AUS (by invitation) I have never seen any benefit from injections of serum in these cases I think the termination of pregnancy is the only "treatment" that offers any prospect of success

**Leprosy, "Neural" Anesthetic, Minimal, and "Neural" Tuberculoid, Severe (Na 1, Nt 3)** Presented by DR HARRY L ARNOLD JR

M K, a 19 year old Hawaiian girl, was first seen on March 10, 1945, because of lesions of the skin which she says have been present only about two months and have looked from the beginning much as they do now

Examination discloses an adequately developed and nourished adolescent Hawaiian girl with a generalized eruption of erythematous plaques, mostly 5 to 15 cm in diameter, on all parts of the body except the palms, the soles and the mucous membranes Many of them have slightly elevated narrow cicatricial borders, many have crusted erosions or shallow ulcers situated within them

There is slight right facial weakness and bilateral thenar and hypothenar atrophy Tactile anesthesia is demonstrable in only one or two small areas on the ankles and the backs of the hands There is no anesthesia to cold except in one or two of the larger plaques There is hyperesthesia and hyperalgesia to heat in much of the normal-looking skin outside the plaques and hypoaesthesia to heat inside most of them

A smear made from a specimen taken for biopsy this morning was negative for acid-fast bacilli

NOTE.—Biopsy subsequently showed sharply circumscribed noncaseating epithelioid cell tubercles scattered throughout the corium, some of them clustered

about the cutaneous appendages The acid-fast stains showed only occasional acid-fast bacilli in some of these foci The histologic diagnosis was tuberculoid leprosy

## DISCUSSION

CAPTAIN HERBERT LAWRENCE, M C, A U S Why did you designate the case as one of neural leprosy?

DR HARRY L ARNOLD JR Because it is leprosy of the type still officially known as "neural," despite the fact that it involves the skin in this case much more severely than it does the nerves The term "neural" in this connection does not refer to nerve involvement, but to the type of the disease in which a strong tissue reaction against the bacillus is present The histologic picture shows epithelioid cell tubercles, and bacilli are scanty or absent except during transitory "reactions" This is what used to be called "maculoanesthetic" leprosy, and the lesions are what were formerly called "leprides"

LIEUTENANT COLONEL CARL F TESSMER, M C, A U S (by invitation) Wouldn't the word "neural" be better omitted?

DR HARRY L ARNOLD JR I think that a better word could easily be found—"tuberculoid," for example—but I am sticking to "neural" because it is still official the world over, and has been since its adoption by the 1931 Conference in Manila and its approval at the 1938 Conference in Cairo A physician in Calcutta or Manila or China or New York should be able to tell just what type of case I am talking about when I say that it is an "Na 1, Nt 3"

DR HAROLD M JOHNSON I still think that Pardo-Castello's classification is the best This one seems too complex to me

MAJOR TIBOR BENEDEK, M C, A U S (by invitation) What will be done with this patient?

DR HARRY L ARNOLD JR In general, patients of this type, in whom bacilli cannot be demonstrated, are merely legally certified as leprosy by a board of three physicians and then recommended for immediate temporary release and observed monthly for two years, quarterly for two years, semiannually for two years and then annually If their lesions become active or if bacilli can be demonstrated, they are hospitalized They are also hospitalized when they need hospital care for any other reason, such as the development of trophic ulcers

DR HAROLD M JOHNSON I certainly would not hear of giving this girl immediate temporary release with those open lesions on her legs She will have to be hospitalized until those lesions heal

## MANHATTAN DERMATOLOGIC SOCIETY

George M Lewis, M D, *Chairman*

Wilbert Sachs, M D, *Secretary*

March 13, 1945

### Neurodermatitis with the Histologic Picture of Mycosis Fungoides Presented by DR. MAX SCHEER

T O, a man aged 38, is presented from the New York Skin and Cancer Unit with an eruption on the upper part of the back, the left ankle and the left gluteal region of four years' duration

The patient presents four lesions in all, two of approximately dollar size on the upper part of the back, which are thickened and scaly, and a palm-sized erythematous lichenified plaque in the region of the left lower gluteal fold, with a lichenified plaque showing exaggerated cutaneous markings covering the outer aspect of the left ankle and extending onto the leg and down on the foot

This patient was originally referred to the Skin and Cancer Unit by Dr Gilson, a former resident, in February 1944. A biopsy from one of the lesions on the back at that time showed the microscopic picture of mycosis fungoides. The patient was not seen again at the hospital until January 1945, when another biopsy was performed because of the seeming discrepancy between the clinical and the microscopic picture. The histologic report confirmed the original data on the microscopic changes.

## DISCUSSION

DR ISADORE ROSEN. On clinical grounds alone I should not consider the diagnosis of mycosis fungoides. There are a few isolated, sharply outlined, superficial, mildly infiltrated patches of lichenoid eczema, and if there were no microscopic report no one would think of mycosis fungoides. I have seen histologic reports from trained pathologists in which a diagnosis of neurodermatitis was originally made, and subsequently the disease proved to be mycosis fungoides.

DR FRED WISE. I fully appreciate the significance of two biopsies, both of which are interpreted as mycosis fungoides, and I know that some cases of mycosis fungoides begin clinically as eczema. From the clinical aspect, the eruption bears no resemblance to mycosis fungoides.

DR THOMAS N GRAHAM. I agree with the previous speakers.

DR WILBERT SACHS. I should like to state that it all depends on what the microscopic changes were. Some microscopic pictures simulate others. One cannot differentiate between certain forms of neurodermatitis, nummular eczema or mycosis fungoides, when the reaction is focal about the vessels. If this slide showed a diffuse process with other findings of mycosis fungoides, I believe that we should have to accept that diagnosis. This is a focal reaction about the vessels, and it may be almost impossible to state whether it is mycosis fungoides or one of the other diseases mentioned.

DR ANTHONY C CIPOLLARO. Clinically the eruption certainly does not have the manifestations of mycosis fungoides, and yet if I had performed two biopsies and both showed the characteristics of mycosis fungoides, I should have to accept that diagnosis, even though it is not clinically suggestive of that disease. I don't even know how to differentiate therapeutically between mycosis fungoides and this type of dermatitis, because both are apt to improve with a few small doses of roentgen rays.

DR WILBERT SACHS. I believe that this is not a simple neurodermatitis, it belongs in the lymphoblastoma group. The epidermis is not that of neurodermatitis. It is a lymphoblastoma, probably mycosis fungoides.

DR E WILLIAM ABRAMOWITZ. I know of no way of differentiating the eczematous stage of mycosis fungoides, especially if it is of short duration, from other types of eczematous lesions, except on histologic grounds. If the biopsy report indicates the features of mycosis fungoides, the patient should be observed with that in mind.

DR GEORGE M LEWIS. I should like to ask Dr Scheer whether it is not unusual to see localized neurodermatitis on so many areas, and particularly on the trunk.

DR JACK WOLF. The clinical appearance of the patch on the outer aspect of the leg and foot is so typical of neurodermatitis that I think that there is little doubt of that diagnosis. I think that the two lesions on the back should be fitted in with that diagnosis, rather than to assume that we are dealing with mycosis fungoides. The lack of progression, the persistence and the lesions, aside from those on the back, all favor a diagnosis of neurodermatitis rather than mycosis fungoides.

DR GIRSCH D ASTRACHAN. Isn't it most unusual for neurodermatitis to be located on the buttocks?

DR MAX SCHEER To my mind, the lesion on the upper part of the back was different from the other neurodermatitis-like lesions. The lesion on the back was red, somewhat infiltrated and sharply defined, and could well pass clinically as early mycosis fungoides. Today that lesion has changed greatly, having retrogressed by 75 or 80 per cent, so that it is clinically impossible to make any diagnosis. Whether the regression is the result of one or two roentgen ray treatments, I don't know. Dr Sims and Dr Sachs both made a histologic diagnosis of mycosis fungoides. Dr Jessner looked at the slide and did not agree at all with that diagnosis. He saw the patient, and said that both clinically and histologically the lesion was banal.

**Multiple Benign Cystic Epithelioma** Presented by DR GIRSCH D ASTRACHAN

F G, a white woman aged 46, born in Hungary, registered at the dermatologic clinic of the Metropolitan Hospital on Feb 2, 1945, with the history of an eruption on the face of thirty-nine years' duration. She also presented an ulcerated lesion on the upper lip which was diagnosed and treated as a basal cell epithelioma. The patient has also been receiving treatment for occasional attacks of epilepsy.

On the face, especially on the forehead, upper parts of the cheeks and behind the ears, are many scattered or closely set skin-colored or pale yellow, elevated, round, smooth, solid or soft lesions, some of which are shiny, translucent and almost vesicular in appearance. The size of the lesions ranges from that of a pinhead to that of a small pea. Some of the lesions have a central depression.

Dr Wilbert Sachs reported that the microscopic picture was typical of multiple benign cystic epithelioma.

DISCUSSION

DR MAX SCHEER I accept both diagnoses.

DR MAURICE J COSTELLO The interesting feature is the extent of the involvement.

DR FRED WISE I agree with the diagnosis and think that it is an unusually interesting example of the disease. The majority of cases presented and pictured in textbooks show the eruptions on the sides of the nose, whereas here most of the eruption is on the forehead and behind the ears.

DR GEORGE M LEWIS Isn't the lesion unusually small?

DR FRED WISE The lesions vary in size.

DR GIRSCH D ASTRACHAN I believe that the most interesting features in this case are the location of the lesions behind the ears and the fact that this patient had a basal cell epithelioma on the face a few months ago. It is possible that the latter developed from one of the lesions of multiple benign cystic epithelioma.

**Darier's Disease** Presented by DR MAX SCHEER

D S, a girl aged 11, is presented from the New York Skin and Cancer Unit with a pruritic eruption on the scalp and the sides of the neck, of one year's duration.

On the sides of the neck the patient presents acute, superficial, erythematous, crusted patches half the size of a palm on each side of the neck above the clavicles, surrounded by many small pinhead-sized, hyperkeratotic, scaly spots. The eruption on the scalp occupies chiefly the top of the head and consists of erythematous and scaly areas which have coalesced to form an extensive reticulated area.

Clinically, the diagnoses of seborrheic dermatitis and eczematized neurodermatitis were entertained. On histologic examination, the typical microscopic picture of Darier's disease was found.

## DISCUSSION

DR WILBERT SACHS The slide which I saw did not show that picture I would not want to venture a positive diagnosis, but on a hasty look would say that it is more like the Hailey-Hailey syndrome than keratosis follicularis. As for the description of the slide, I do not believe that the cells are the same in keratosis follicularis (Darier) as in so-called bullous Darier's disease. The cytologic picture is entirely different.

DR MAURICE J COSTELLO From the clinical point of view, it is a case of what I consider ordinary Darier's disease.

DR THOMAS N GRAHAM I agree that this case appears to be keratosis follicularis as described by Darier. Although the microscopic picture may be that of the Hailey-Hailey syndrome, it does not suggest this dermatosis clinically.

DR FRED WISE I think that it is Darier's disease.

DR E WILLIAM ABRAMOWITZ I should be inclined to favor the diagnosis of Darier's disease. Dr Rosen's suggestion of a possible favus or other parasitic infection should be investigated.

DR MAX SCHEER When the patient was first seen at the clinic I never thought of Darier's disease. On the sides of the neck it appeared to be dermatitis. When this had subsided, as it has to a considerable extent, one could see small keratotic papules which clinically are those of Darier's disease. The histologic picture was reported by Dr Sims as Darier's disease. However, there is no familial history and at no time did we see vesicles, even at the time of the dermatitis. As I recall the slide, there was a split in the epidermis paralleling the surface of the skin, and a few corps ronds. I think Dr Sims and Dr Sachs are practically in agreement as to the histologic picture. I should rather be guided by the clinical picture tonight, which I believe is that of Darier's disease.

**Infectious Eczematoid Dermatitis** Presented by DR MAURICE J COSTELLO

A P, a woman aged 26, was admitted to Bellevue Hospital on Jan 4, 1945. Shortly before this an abscess developed on the right side of the patient's neck, which was incised and drained. About one week later pruritus developed on the right side of the neck, the scalp, the axillas, the intermammary areas and the pubes. The patient states that she had been admitted about four months previous to the present occasion, at which time she had a dermatitis in the same locations, and that an exacerbation took place after the abscess developed. On each occasion she has had otitis media with drainage involving the right ear. At present there is some involvement of the left ear.

The patient states that in 1942 she had a permanent wave and that her scalp was burned in the process. In May 1943, when she gave birth to a child, she noticed that the axillas, the intermammary areas and the pubes were inflamed and pruritic.

Examination on admission showed an inflammatory, erythematous, somewhat infiltrated involvement of the skin of the scalp, the neck, the right ear and the upper portion of the forehead with areas of serous exudation. The axillas and the pubes showed many pinhead to pea-sized papules and pustules superimposed on a diffuse inflammatory base. The intermammary areas showed a diffuse erythema with serous exudation. The right external auditory meatus was acutely inflamed and contained a seropurulent discharge. Beneath the right ear was seen a circumscribed, infiltrated, erythematous mass, slightly elevated and tender to pressure. There was anterior and posterior cervical adenopathy. Enlargement of the thyroid gland was noted.

The Wassermann reaction of the blood was negative, and the urine was normal. The blood count showed 4,700,000 erythrocytes and 12,000 white blood cells, with 65 per cent polymorphonuclear leukocytes, 22 per cent lymphocytes, 11 per cent

eosinophils and 2 per cent basophils. A culture of the secretion from the neck was negative.

Treatment consisted of penicillin to a total of 2,000,000 units, fever therapy—typhoid, single vaccine, and topical applications.

#### DISCUSSION

DR ANTHONY C CIPOLLARO The differentiation between seborrheic dermatitis and of infectious eczematoid dermatitis has always been a puzzle to me. The various tests which attempt to distinguish between the two eruptions are not sufficiently critical to be truly diagnostic. These diseases are tremendously recalcitrant to treatment. They do best under the application of wet dressings, combined with roentgen therapy. I should not hesitate to use small doses of roentgen rays in limited quantities to the region of the scalp.

DR GIRSCH D ASTRACHAN The clinical manifestations in this case impress me as being those of seborrheic dermatitis, however, there are also some features suggestive of infectious eczematoid dermatitis. I should suggest the use of large doses of crude liver extract, given intramuscularly, three times weekly, combined with the oral administration of vitamin B complex. I have seen patients improve under this therapy.

DR WILBERT SACHS Dr Costello has been studying this patient, and we have to accept his diagnosis. I should not have thought of seborrheic dermatitis, but of a *Monilia* infection.

DR THOMAS N GRAHAM The case impressed me as being one of seborrheic dermatitis with secondary infection, rather than one of acute infectious eczematoid dermatitis, which is usually secondary to a focus of infection. If the disease were infectious eczematoid dermatitis, I think that it would probably have responded to penicillin.

DR FRED WISE I have no useful suggestions regarding treatment, but I can say that in my experience the great factor in curing disease like this is time—months and months of rest in bed. There is no specific treatment.

DR ISADORE ROSEN I should suggest the diagnosis of psoriasis with a superimposed secondary dermatitis. The sharply outlined lesions involving the scalp and the postauricular and pubic areas always suggest psoriasis, to my mind. In this case the eczematization of the lesions is due to secondary effects.

DR E WILLIAM ABRAMOWITZ These cases are a problem to all of us who have occasion to give treatment for them. The patients finally get well if given sufficient time. I consider infectious eczematoid dermatitis an entity although it favors the location of the seborrheic areas and occasionally resembles psoriasis. A suppurating focus is usually present somewhere. A troublesome feature is discharge from the ear canals, and the question arises of a purulent otitis media as the cause. Dr Morris Levine of the Ear Department of the New York Post-Graduate Hospital has cooperated with me in several such cases, and he proved to my satisfaction that the involvement of the ear canal is due to the extension of the infectious dermatitis from the skin. Perforation of the tympanum may occur, and then, of course, there is continuous discharge establishing a vicious circle. Radical measures are unnecessary. Frequent dry cleansing of the ear canal, and trial of penicillin ointment or other antiseptic measures may prove beneficial. Penicillin by injection and bacteriophage therapy have not been helpful.

DR GEORGE M LEWIS I think that the diagnosis of infectious eczematoid dermatitis is correct.

DR MAURICE J COSTELLO This patient has been under my observation for almost a year, and I should state that she has gone through all the stages mentioned by Dr Abramowitz in his discussion. The so-called focus of infection in the middle ear is, in reality, an extension of infection from the skin of the external ear. The patient first presented severe seborrheic dermatitis involving the posterior auricular region, the scalp, the axillas and the inframammary and pubic



regions. The eruption finally became so severe that the patient was admitted to Bellevue Hospital. Four million units of penicillin were administered, and the eruption cleared remarkably. The patient was discharged, but later called me and said that she had a large abscess in the neck. She was taken to a hospital in Brooklyn, where the abscess was incised and drained. She was later readmitted to Bellevue Hospital, where she was treated with application of dyes, penicillin ointment, etc. The second time penicillin was given intravenously, and the eruption did not improve greatly. The patient was referred to the Nose and Throat Department, where a diagnosis of otitis media was made. I have seen a number of patients with this condition.

#### **Dermatitis Medicamentosa (Quinacrine?)** Presented by DR JACK WOLF

M. R., a man aged 34, was recently discharged from the army because of the eruption for which he is being presented tonight. He registered at the New York Skin and Cancer Unit this morning. The first signs of dermatitis appeared eight months ago when he was stationed in New Guinea. The eruption grew progressively worse, and spread to involve the entire cutaneous surface. He was hospitalized for several months in the Pacific area and then in a nearby base hospital. There has been some improvement during the past few weeks. One of the patient's chief complaints is that he is unable to perspire and is made extremely uncomfortable thereby. The only pertinent history elicited is that he was taking quinacrine hydrochloride at the time the eruption appeared and for several months prior to that. Other soldiers in his group experienced similar but, in most instances, milder eruptions.

The eruption is widespread and severe, involving the head, the neck, the torso and the extremities. The most pronounced lesions are present on the face, the scalp and the ears, these are numerous lentil-sized and somewhat larger depressed, atrophic, shallow, erythematous and telangiectatic spots. The depigmentation of the atrophic spots and the surrounding hyperpigmentation impart a mottled appearance to the face. The extensive involvement of the scalp has caused almost complete loss of hair in the temporal and occipital regions and on the vertex. The reddish atrophic spots, as well as erythema and telangiectasis of the rest of the skin, are present on the extremities and to a lesser degree on the torso. The vermilion borders of the lips are affected and are dry and whitish in spots and show considerable telangiectasis. There is extensive irregular leukokeratosis of the buccal mucous membrane and to a lesser degree on the tongue.

#### DISCUSSION

DR MAURICE J. COSTELLO: I agree with the diagnosis. I had an opportunity to see a similar picture in Dr. Howard Fox's office, in a soldier just returned from the Pacific with a generalized eruption which strongly resembled annular lichen planus. The lesions were generalized, solid and coin sized, and some had atrophy and hyperpigmentation. I think that it was caused by quinacrine.

DR DAVID BLOOM: A few months ago I treated in my office a patient with an annoying lingua geographica. This man, who had been in the armed forces in the South Pacific, presented an eruption identical with that shown by Dr. Wolf's patient. The generalized pigmented eruption with lesions on the oral mucous membrane and the history of severe pruritus suggested strongly the diagnosis of lichen planus. The unusual feature, as in the case presented tonight, was the considerable scarring of the face. I believe now that that case was most probably the result of prolonged ingestion of quinacrine.

DR E. WILLIAM ABRAMOWITZ: Cutaneous reactions were reported when quinacrine and pamaquine naphthoate were first introduced. The type of eruption that this patient presents is reminiscent of that encountered after the prolonged use of the arsenicals, gold and bismuth preparations and thallium acetate. Further observation is necessary to determine the causal relationship.

DR ANTHONY C CIPOLLARO Most of the members agree that this is a drug eruption, and there is a definite history that this person has been taking quinacrine. It is a quinine-like substance, and like quinine is apt to be a photosensitizer. The patient took the drug in an environment and atmosphere where he was constantly exposed to the sun. This photosensitivity is probably responsible for the appearance of different types of lesions. The patient has two other conditions that are seen in men who have returned from the South Pacific regions, namely, areas of depigmentation and loss of sweat function. So if we conceive of this as being a drug eruption caused by a photosensitizing drug, in a person who had to be constantly exposed to the sun, I think that it would explain the multiplicity of the lesions.

DR JACK WOLF Because the patient was seen for the first time this morning, we have not had the opportunity of doing any investigative work. The clinical resemblance to lupus erythematosus, especially on the face, suggests that we may be dealing with the photosensitization effects of quinacrine on the human skin.

### LOS ANGELES DERMATOLOGICAL SOCIETY

A Fletcher Hall, M D, *Chairman*

Clement E Counter, M D, *Secretary*

*March 13, 1945*

**Angiolupoid of Brocq and Pautrier** Presented by DR FLETCHER HALL

G E is a married white woman aged 47 years. A small purplish red crusting area developed at the base of her nasal septum six weeks ago. Mentholatum (10 per cent camphor, 10 per cent boric acid, 1 per cent menthol, about 0.3 per cent oil of eucalyptus, about 0.3 per cent oil of wintergreen, about 0.3 per cent oil of pine needles, and white wax and white petrolatum) and ammoniated mercury ointment were used locally. The lesion continued to spread to the present size. The patient has lost about 8 pounds (3.6 Kg) since the onset of the eruption.

Her younger sister had tuberculosis when the patient was 18 years old.

A continuous plaque consisting of a confluence of irregularly elevated purplish red rounded smooth-surfaced papules, varying from the size of a pinhead to that of a small pea, are on the upper lip, the cutaneous portion of the nasal septum, the mucocutaneous junction of the external nares, the skin just lateral to the oral commissures, the nasolabial folds and the chin. The borders of the lesions are defined and irregular in contour. The elevated papules are of rubbery consistency. The skin immediately adjacent to the mucocutaneous junction of the lips is free from involvement, as are the mucous membranes. There are no local lymph nodes palpable. There is a small, ill defined group of similar but smaller lesions on the right lower eyelid. Diascopic pressure shows a mottled brownish yellow pigmentation but no discrete apple jelly nodules.

The Eagle and Kline tests of the blood were negative. Roentgen examination of the chest showed a few calcified peritracheal nodes but no evidence of present or recent tuberculosis.

The microscopic section showed a thin epidermis with few partly flattened papillae. The upper part of the dermis showed considerable vascular dilatation and a massive infiltrate which consisted mainly of epithelioid cells, some giant and a few plasma cells. In the deeper layers of the dermis connective tissue cell proliferation was present as well as many nests of epithelioid cells. No caseation was present.

### DISCUSSION

DR M E OBERMAYER This case is one of lupus vulgaris. The history of so short a duration as six weeks would ordinarily rule this out, but I have nothing

else to suggest. Sarcoid can be ruled out from the slide. It is a chronic infectious granuloma.

DR H C L LINDSAI: The area involved has increased too rapidly for lupus vulgaris. Syphilis should be considered.

DR KENDAL FROST: I agree with Dr Obermayer that it is a chronic infectious granuloma, but I do not think that it is tuberculosis.

DR SAMUEL AYRES JR: Especially in California, where lupus vulgaris is a rare disease, it does not seem reasonable for such a disease to develop with that rapidity with no obvious source of infection. In this absence of an obvious focus I don't see how you can make a diagnosis of lupus vulgaris.

DR A FLETCHER HALL: It is difficult for me to accept lupus vulgaris as a diagnosis in this case for the reasons Dr Ayres brought out as well as because of the fact that diascopy does not show nodules of the apple jelly type. There is tuberculosis in this patient's family history, and she is supposed to have had "inflammation of the lungs" as an infant. Roentgenograms of the chest do not show any evidence of present or recent tuberculosis. The description of "Angiolupoid" (Brocq and Pautrier) as set forth in McCarthy's text, "Histopathology of Skin Diseases," tallies with the clinical and microscopic findings in this case. It is listed with the tuberculous eruption, although its tuberculous origin has never been proved. Although I am not familiar with that disease, I favor tentatively classifying my case as an example of it.

#### **Leprosy, Tuberculoid Type** Presented by DR SAMUEL AYRES JR

R H is a Korean man aged 61 years. He became aware of a lesion on the right arm nine months ago, and he attributed this to an injury of his right hand one year ago. After two months the injury appeared to be well, but the present eruption began to develop on the arms, the face and the trunk. The patient has not been out of the United States during the past thirty years but has lived in California or Arizona during that time.

The most conspicuous lesions are on the face, but lesions are also present on the arms and trunk. On the lower portion of each cheek is a sharply defined, erythematous plaque slightly paler centrally with darker and more infiltrated periphery. There are three small but similar lesions on the right side of the neck and chin and above the right eyebrow and within the left eyebrow. There also are lesions scattered over the arms and forearms and several lesions on the trunk, especially on the back. The patient stated that the lesions above the right eyebrow had been present since childhood, following an injury. There are two healed scars on the flexor aspect of the right thumb and the index finger at the site of the injury occurring one year ago. The lesions are anesthetic to pain.

A positive reaction was produced with the histamine test. The reaction to the Mitsuda test was positive after forty-eight hours. Acid-fast bacteria were not present in nasal smears. A biopsy showed extensive infiltration, especially through the upper cutis, with masses of epithelioid cells and small round cells, and large giant cells had a tendency to be arranged in masses.

#### **DISCUSSION**

DR M E OBERMAYER: This case was a good illustration of the tuberculoid form of leprosy. The clinical features and the positive reaction to the Mitsuda test indicate that it is a benign type of the disease.

As the forms of leprosy once established do not change, the prognosis for this patient is good, and since he is not a bacilli carrier he does not endanger the community. I believe that there will soon be a change in the handling of isolation measures. Only patients who have the lepromatous form of the disease will be isolated, while the ones with the tuberculoid type will be allowed to remain where they are. By the same token, the patients who have tuberculoid leprosy are not "true contacts" as far as follow-up measures are concerned. E G, the wife of this patient, is not likely to acquire leprosy from her husband for the simple

reason that his form of the disease is, for practical purposes, noninfectious, hence, the term "false contact" which is used in Mexico in follow-up investigations to designate the patient with tuberculous leprosy, in contrast to the "true contact," the patient who has the lepromatous form of the disease

The Mitsuda test is an all-important diagnostic measure, because it aids in the classification of the disease. The book which I am passing around is the most comprehensive study published on the subject (Zurita, F H. *La reaccion de Mitsuda*, Universidad Nacional Autonoma de Mexico, Facultad de Medicina, Mexico, D F, Mexico, 1943). The Mitsuda test indicates whether or not a defense mechanism against the disease has developed. Therefore it is the patient with a negative reaction who not only offers a poor prognosis but who also is a danger to the community. While the lepromatous (nodular) form of the disease is most commonly encountered among lepers with negative reactions, I was shown cases in Mexico by Dr F Latapi of the unusual so-called diffuse form of leprosy, in which the skin may look almost normal. Patients with this form of the disease have abnormal reactions to histamine all over the body, and bacilli are easily demonstrated.

DR LOUIS G JEKEL. This patient gave a history of having lived in Arizona. It occurred to me that Dr McCoy of the United States Public Health Service told me in 1938 that up to that time he had had no record of any case of leprosy originating in Arizona. In my seven years' practice there I have seen only 1 such case. The patient was a Mexican citizen who had been sent into Arizona to do farm labor and whose illness began before he left Mexico.

DR SAMUEL AYRES JR. All facts presented agree with the opinion that this case is one of benign type. The positive reaction to the Mitsuda test and the lack of organisms in the stained tissues especially emphasize the benign character of the patient's disease.

#### Cutaneous Scopulariopsis. Presented by DR FLETCHER HALL

H L E is a white man aged 39 years. Twenty-four years ago an abdominal paracentesis was performed. Three gallons (11.4 liters) of ascitic fluid was obtained. He was told he had "miliary tuberculosis." This was seven years before the onset of the present eruption. There has been no recurrence of fluid in the abdomen. This patient was presented before this society in December 1944 as possibly having blastomycosis, although no *Blastomyces* was demonstrated by direct microscopic examination, culture or biopsy. At that time the diagnosis of hypertrophic lupus vulgaris or some other form of tuberculosis cutis was also suggested.

Since that time a tuberculin patch test produced a severe reaction, but a triturate of a large amount of material excised from the active border of the lesion and injected intraperitoneally into a guinea pig did not demonstrate the presence of the tubercle bacilli. The guinea pig gained weight and showed no evidence of pathologic changes on autopsy six weeks later. Acid-fast stains of tissues removed for biopsy showed no tubercle bacilli. A pure culture identified as *Scopulariopsis* (Markley, Philpott and Weidman, *ARCH DERMAT & SYPH* 33:627-741 [April] 1936) was grown on Sabouraud's medium.

Since December 5 the lesion has received thirteen treatments with unfiltered roentgen rays. Each treatment consisted of 75 to 100 r. He has been taking 50 to 80 drops of saturated solution of potassium iodide three times daily. Since this treatment was instituted great clinical improvement has taken place. There is greater improvement in the anterior half of the lesion. The posteromedial border still shows verrucous hypertrophy.

The patient is presented tonight to show the improvement from iodide and roentgen therapy, and to report on further laboratory studies.

#### DISCUSSION

DR H P JACOBSON. To help in the determination of an etiologic relationship of the growth in the culture shown tonight a filtrate of the organism in bouillon

should be prepared for the purpose of cutaneous testing. Should the results prove positive, then a properly prepared autogenous vaccine might be helpful in the treatment of the case.

DR ORDA PLUNKETT (by invitation) The genus *Scopulariopsis* contains six or eight species which have been reported as pathogenic. Several reports have been made of infections of nails and also of the outer ear. Some have been isolated from deep-seated lesions. In 1 case the author reported isolating a species of *Scopulariopsis* from a deep-seated blastomycosis lesion. Most species of this genus are saprophytic. Some are fond of growing on protein substances, some cause spoilage of cheese, and others are found on decaying vegetation. This species is not identical with any of the eight or ten species taken from sputum, ears and plates exposed to air. Neither is it the same as any of the well known saprophytic species. It may be a pathogenic form. I injected the material into 5 rats subcutaneously and intratesticularly. I killed 1 after three weeks and found no evidence of any sign of tissue disturbance in the tests. There was a small walled-off abscess where I had made the subcutaneous injection, but I did not isolate the organism from it. Unfortunately the other 4 rats were disposed of by mistake without examination.

DR H C L LINDSAY It is an area of considerable proportion, and if the disease were blastomycosis or syphilis one would not expect any new papules of infection springing up in the old scar, such as in this case. Under ordinary circumstances one would expect this lesion to be tuberculosis.

DR A FLETCHER HALL We certainly have suspected tuberculosis here, not only because of the microscopic appearance but because of the fact that this man has a history of tuberculous peritonitis, a large amount of ascitic fluid was withdrawn by paracentesis and he was told that he had a milary tuberculosis. A tuberculin patch test performed two months ago resulted in so strongly positive a reaction that he still has the mark on his arm. Material injected into a guinea pig, however, did not produce tuberculosis, because presumably it takes only a few organisms to call forth a strong reaction in the presence of such a high degree of sensitivity to tuberculin. Another argument against tuberculosis is that the lesion has improved so greatly under treatment with potassium iodide and roentgen rays.

#### **Exudative Discoid Lichenoid Chronic Dermatitis** Presented by DR MOLLEURUS COUPERUS

S Y is a young man aged 21 years. He is Jewish and was born in the United States.

This eruption began about seven years ago. It was generalized then. The disease has been almost continually present since that time. He noticed that the eruption gets worse in the winter and improves in the summer.

The eruption is generalized. Individual lesions consist of discrete firm round papules varying from the size of a pinhead to that of a match head. In addition to these, there are oval-shaped patches approximately 2 by 3 cm which are urticarial in nature, and some of which are scaly and crusted. These are chiefly located on the chest, the back and the thighs. On the right anterior surface of the thigh there is a large palm-sized plaque of firm lichenoid papules.

Numerous allergic cutaneous tests have been reported negative. The Wassermann reaction of the blood was negative. The specimen taken from the back for biopsy showed considerable parakeratosis with acanthosis of the rete pegs. The papillary bodies were flattened, and there was some edema around the capillaries. Also in the upper part of the cutis there was considerable perivascular infiltrate occurring in "bandlike" arrangement and consisting mostly of lymphocytes and plasma cells.

Treatment has included roentgen therapy, ultraviolet irradiation, fever therapy by typhoid vaccine, intravenous injections and coal tar ointment applied locally, all without benefit.

## DISCUSSION

DR NELSON PAUL ANDERSON From what has been written on this entity, I should not be inclined to accept the present eruption as an example of it. Do these patients have peculiar waxy, lichenoid lesions like those on this man's thigh? Isn't there usually decided involvement of the external genitalia in this disease?

DR MOLLEURUS COUPERUS The waxy papules are unusual, and the age of this patient is unusual. Otherwise I think that the patient is comparable with those whom I have seen in New York. The changes in his face are characteristic of this disease. When Dr Sulzberger and Dr Garbe reported the first 9 cases of this disease in 1937 (*ARCH DERMAT & SYPH* **36** 247-272) all the patients, I believe, were Jewish, and the youngest was 32 years of age. This makes this patient unusual because he has had the eruption for seven years and is now 21 years old. I do not know whether it is usual for these patients to improve in the summer or not. The eruption is characteristic of the disease. I saw the patient in Bellevue when he was there for typhoid treatment of this particular dermatosis. The patient was advised to go west, and he thinks he does best in Arizona.

## Book Reviews

**Dermatología y sífilografía** By Professor V Pardo Castello and others  
Third edition Price \$20 Pp 1492 Habana, Cuba Cultural, S A, 1945

The appearance of a third edition within four years of the publication of the second edition of "Nociones de Dermatología" by V Pardo Castello is an indication of the welcome and appreciation accorded to this outstanding textbook by students and clinicians in Spanish-speaking countries. It is most unfortunate that no translation is available in English for the wider dissemination of a number of ideas and certain points of view, especially in regard to cutaneous diseases of the tropics. In the preparation of the second edition Prof Pardo Castello invited the collaboration of some of his Cuban colleagues. In the third edition he has extended this to include outstanding contributions from other Latin-American countries. The result has been most fortunate and gives to the work an increased variety of specialized viewpoints.

In the present volume the author has endeavored, as far as possible, to employ the classification of the dermatoses according to etiologic factors, retaining for didactic purposes in certain cases the anatomic, histologic and topographic bases of classification when these have practical value. The portion devoted to leprosy emphasizes the histologic and immunologic classification, first conceived by Brazilian and Argentine dermatologists, which is of great diagnostic and prognostic value. The immunologic reactions found in leprosy are discussed in detail, and the technics and interpretations of the histamine and lepromin tests are well discussed.

The chapter entitled "Cutaneous Capillaritis," by Prof Jose Luis Carerra, of Buenos Aires, Argentina, in which the author formulates a classification of certain cutaneous diseases on the basis of the histologic study of primary capillary changes, is a valuable contribution to the understanding of such disorders as purpura annularis telangiectodes and the progressive pigmentary disease of Schamberg. The chapters on pinta, verruga peruana and frambesia tropica are succinct and exceedingly well written by outstanding authorities and provide excellent introductions to the latest thinking in relation to these diseases.

The typography, paper and binding are excellent, as are the numerous black and white photographic illustrations. Unfortunately, the color plates have not been so well reproduced. The work as a whole compares favorably with the best textbooks in any language. It ably reflects the excellent scholarship and the sound clinical judgment of leading dermatologists of Latin America.



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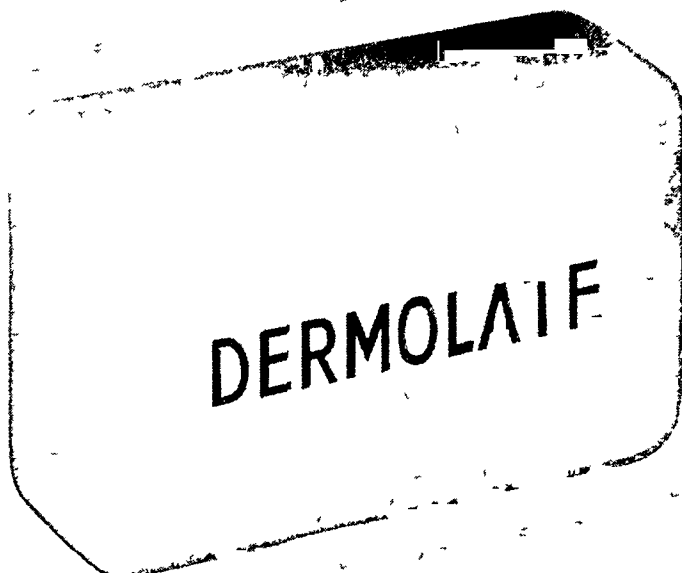
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<sup>1</sup> I. H. Blank, *Arch. of Derm. and Syph.*, 39: 811-824 (1939).  
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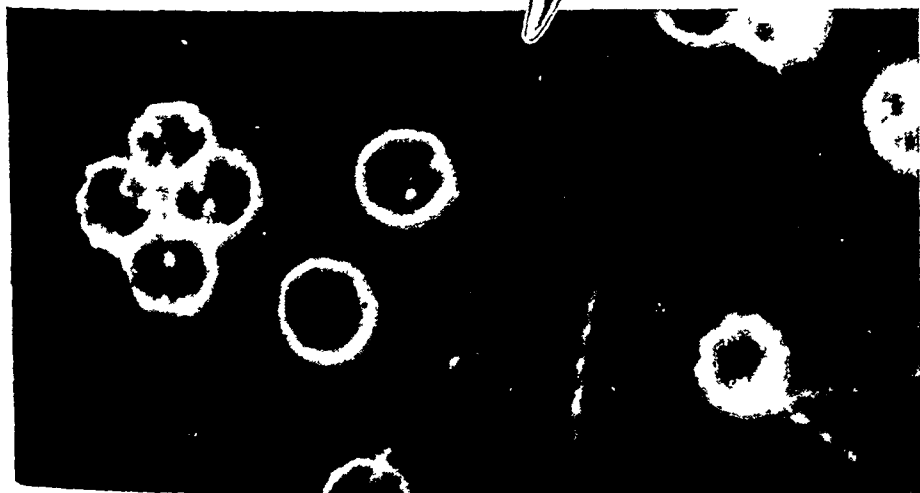
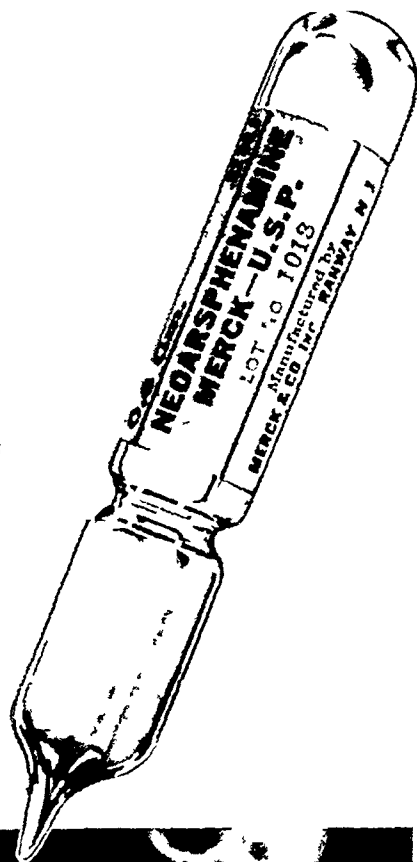
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\*Padget, P, Long-term results in treatment of early syphilis, J. A. M. A. 116:7-11, 1941

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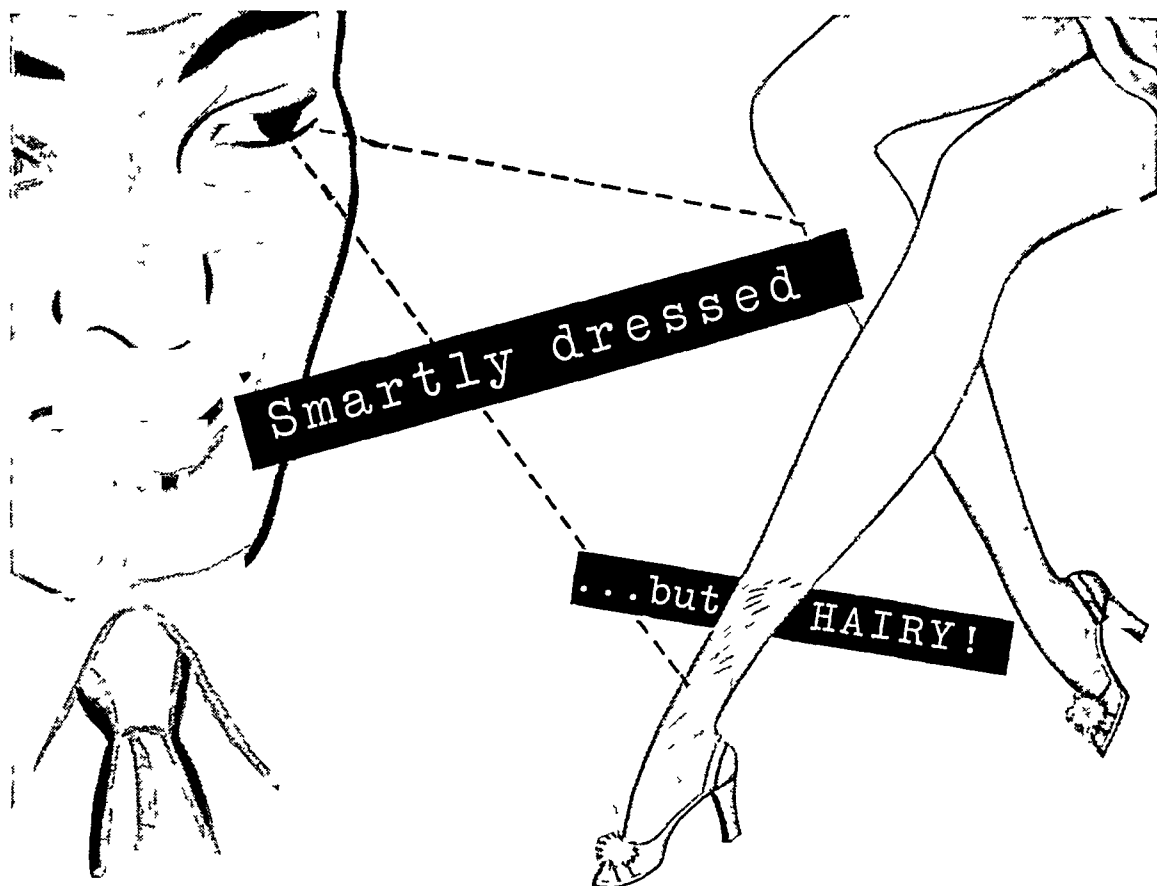
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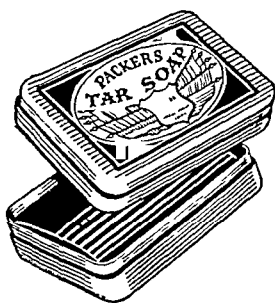
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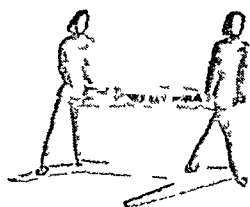
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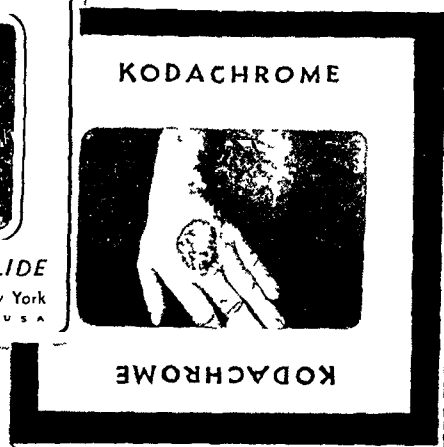
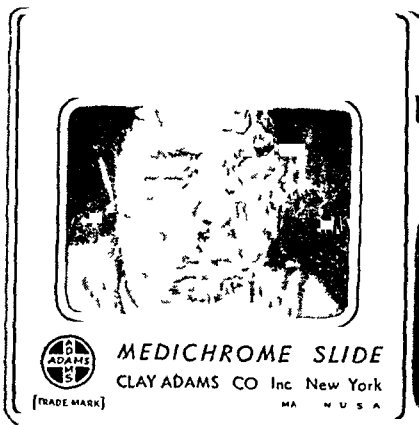
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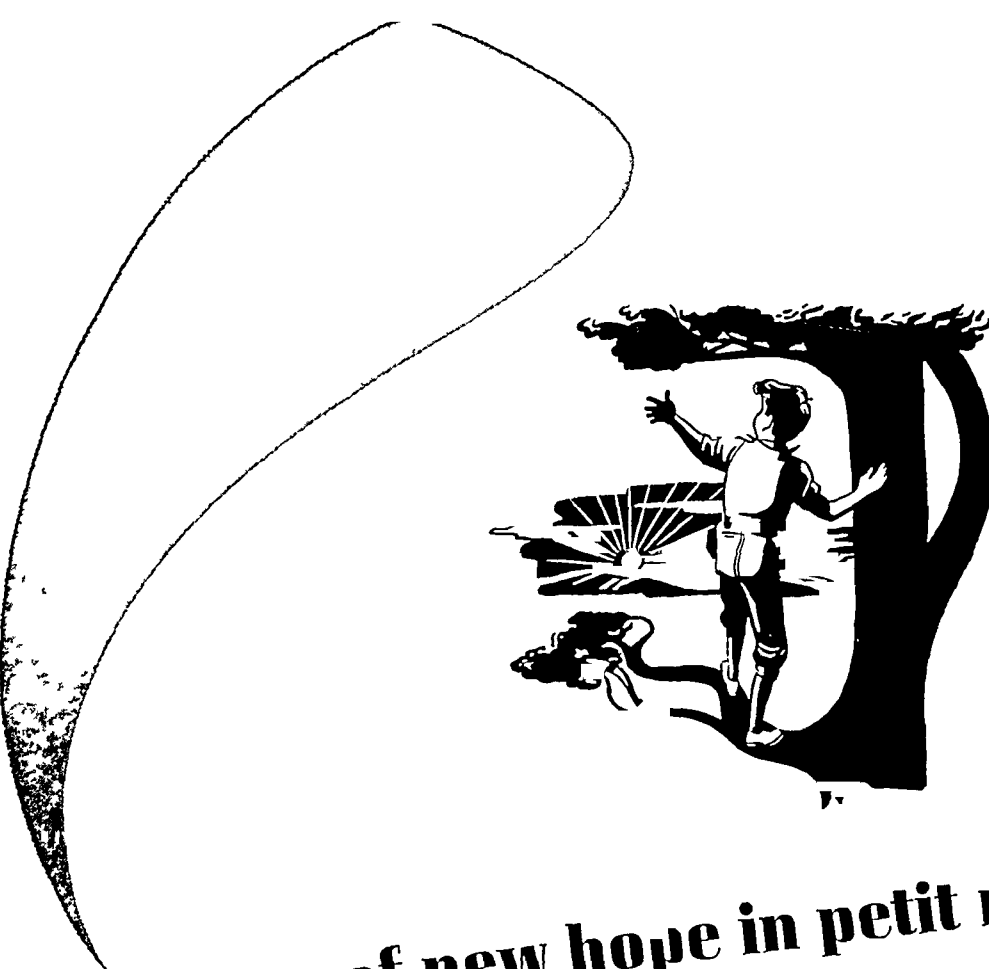
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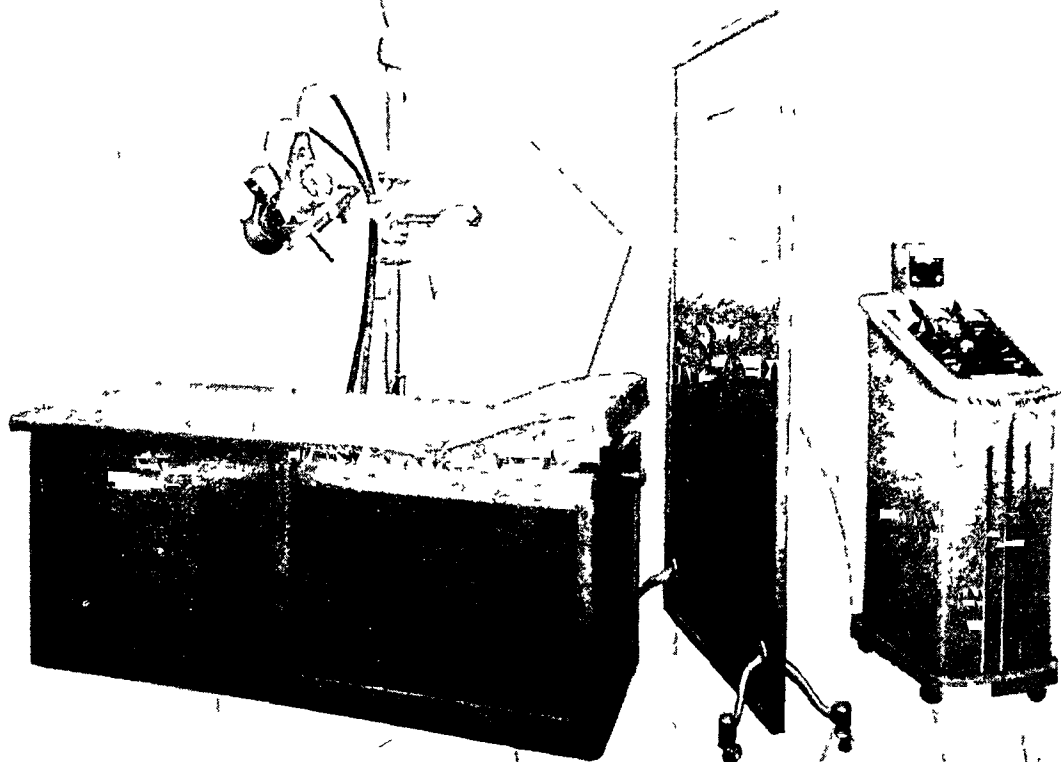
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<sup>1</sup> Lennox, W. G. (1945), *Petit Mal Epilepsies Their Treatment with Tridione*, J. Amer. Med. Assn., 129:1069, December 15.  
<sup>2</sup> DeJong, R. N. (1946), *Effect of Tridione in the Control of Psychomotor Attacks*, J. Amer. Med. Assn., 130:565, March 2.

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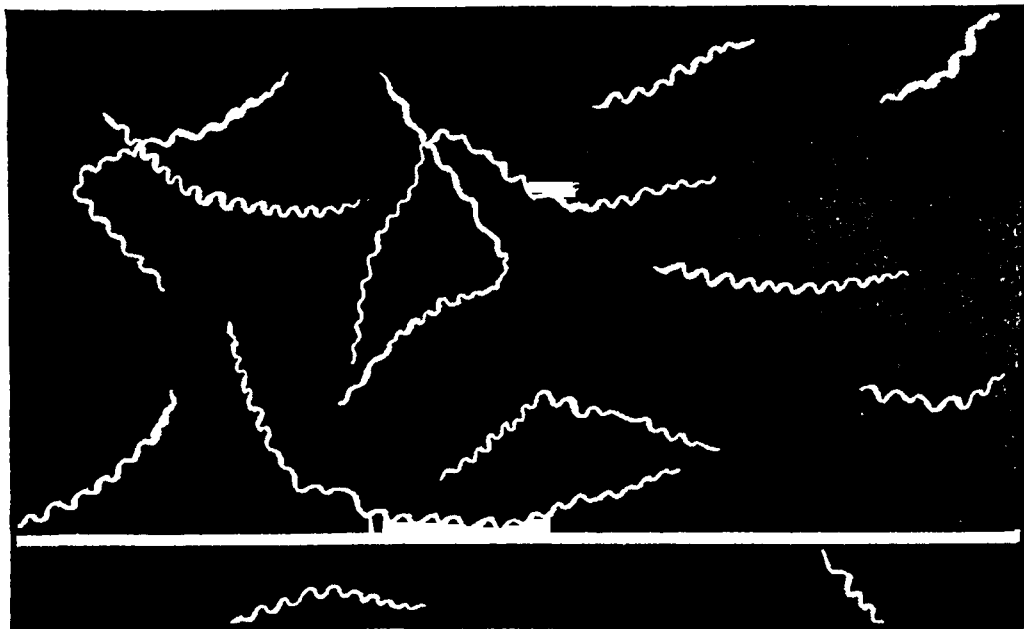
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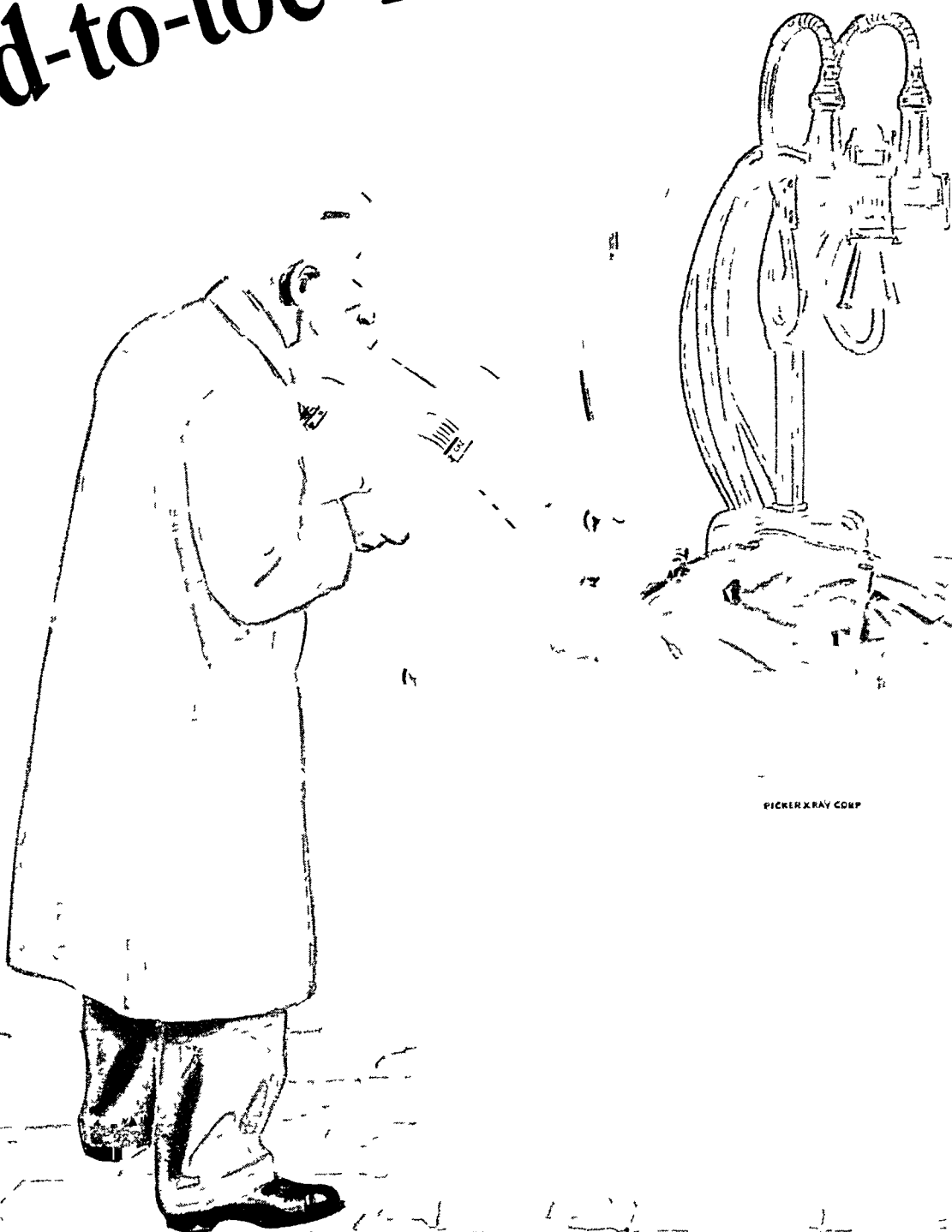
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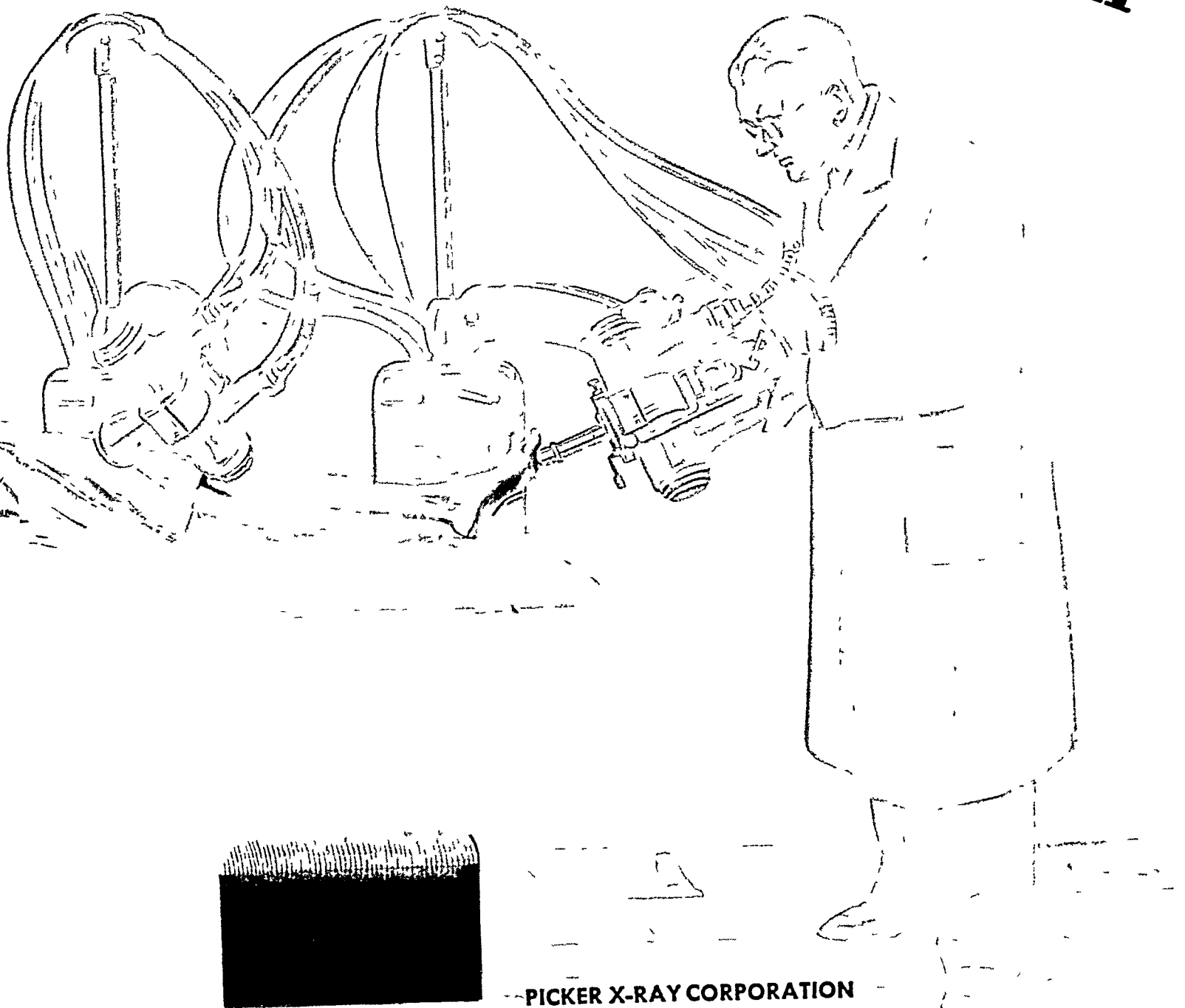


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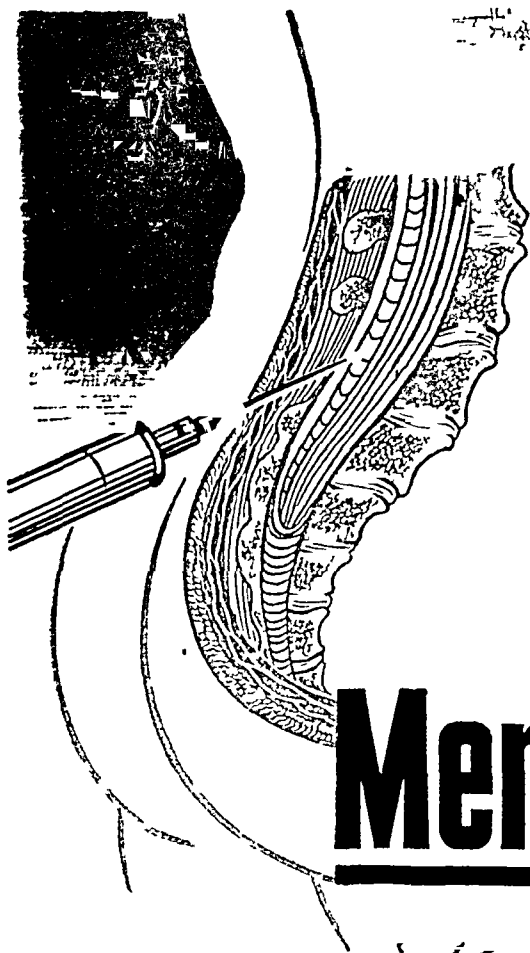
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SPINK, W. W., and HALL, W. H. *Penicillin Therapy at the University of Minnesota Hospitals 1942-1944*. *Ann. Int. Med.* 22:510 (April) 1945.

WHITE, W. L., MURPHY, F. D., LOCKWOOD, J. S., and FLIPPIN, H. F. *Penicillin in the Treatment of Pneumococcal, Meningococcal, Streptococcal and Staphylococcal Meningitis*. *Am. J. Med. Sc.* 210:1 (July) 1945.

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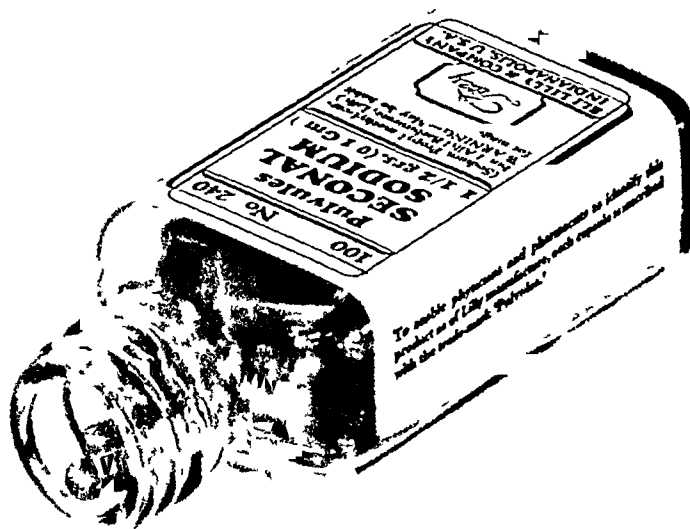
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# Archives of Dermatology and Syphilology

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## ECZEMATOUS AND PIGMENTARY LICHENOID DERMATITIS

Atypical Lichen Planus, Preliminary Report

LIEUTENANT COLONEL DONALD J. WILSON  
MEDICAL CORPS, ARMY OF THE UNITED STATES

SEVERAL surprises greeted the military dermatologist when he first saw and tried to treat patients with "infectious eczematoid dermatitis" from the Southwest Pacific Area. The eruption was resistant, even mild eczematous lesions were characterized by exacerbations, purplish to almost coal black splotches of hyperpigmentation were common, exfoliative dermatitis was not uncommon, severe unexpected complications were not rare, follicular hyperkeratoses were the rule and one group of patients had a disease which closely simulated lichen planus with lesions of the mucous membrane and skin. It seemed entirely likely that in all the cases there was a common denominator. It is my desire to describe the various manifestations of the disease, to record my observations in over 300 cases and to comment on its causation.

This disease, protean in its manifestations, was at first thought to arise only in the New Guinea Area. Cases have now been observed also from the Mediterranean Theater, and although the number is small the clinical characteristics are identical.

### TYPES

On the basis of clinical features, the eruptions can be divided into the dry type, comprising approximately 20 per cent of the cases from the Southwest Pacific, and the exudative type, comprising 80 per cent. Too few cases from the European Theater have been observed by me to permit a determination. Either type may be mild or severe, and both may present complications. Both types may be present in the same person and at the same time. In some cases the lesions first are dry and then become eczematous and again are dry when the patients arrive at the general hospitals in the Zone of the Interior. Dry lesions usually become eczematous if overtreated. Among recent evacuees from the Southwest Pacific Area there is an increasing percentage of eczematous eruptions and the eruptions are much less severe. This is probably due to

From the Medical Service, Dermatology Section, Schick General Hospital, Clinton, Ia.



earlier hospitalization, fewer attempts to return the soldier to duty and earlier evacuation. Many of the patients with severe eruptions received earlier had been given five or six trials at duty between hospitalizations. Many of the earlier patients with eczematous lesions after improving in the hospital were given furloughs in Australia, where the eruptions of a large percentage improved greatly or cleared entirely. On their return to New Guinea, a large number had recurrences before they could rejoin their units. In many patients, oozing disappeared within three or four days after they had left the tropics.

*Dry Type*—Dry lesions frequently begin as indefinitely outlined, pruritic, erythematous, slightly scaling eruptions of the webs of the fingers, on the medial surfaces of the thighs, the palms and soles, the dorsa of hands or feet and occasionally on the face. When first observed in this country, the skin in most cases presents mild to severe dryness, usually of the extremities, with discrete and grouped keratotic follicular papules. Many of the papules present central hyperpigmentation. Many present also indefinitely outlined splotches of pigment about and between the clustered papules. In cases of the more advanced disease there may be present a generalized eruption of the same type, except severer with coalescence of the follicular elements within the patches and increased hyperkeratosis forming variously sized nodules (the largest I have seen were the size of a large hazelnut), covered with a dirty gray, tightly adherent scale. These nodules resemble rather closely the lesions of hypertrophic lichen planus, they often have a deep purple cast and are sometimes angular. I, however, have never seen the phrynoderma of the new disease in conjunction with true lichen planus. In the new disease I have never seen the "cobweb" network so typical of a lichen planus papule. However, a peculiar network is often observed in the atrophic scarlike residuals of healed lesions (fig 1).

A number of patients present lesions of the mucous membrane which are clinically indistinguishable from classic lichen planus with discrete and confluent, milk white macules and papules, bars, circles and segments of circles and plaques. Some of the plaques, especially on the tongue, are intensely painful, decidedly hypertrophic, angular in outline, sharply margined and immediately surrounded by a deep, bright red fissure which bleeds easily.

Nodules resembling those of folliculitis decalvans but with more inflammatory reaction, more hyperkeratosis and less atrophy frequently occur on the scalp and result in alopecia. No patient with alopecia was under my observation for more than four months, and growth of hair had begun again in all but 2. In several the growth was scanty and devoid of pigment.

Some lesions present even more coalescence, resulting in large indefinitely outlined thick plaques covering the dorsa of the hands, dorsa of the feet, shins, legs, buttocks and arms (fig 2).

The nodular lesions slowly clear, with or without treatment, and I cannot state that any local treatment is of value. It was not unusual to see all lesions completely flatten, except one or two, which looked much like soft fibrous nevi but with more pigment. These lesions were



Fig 1—Blond soldier from Mediterranean Area in whom extensive grouped follicular hyperkeratoses developed but did not progress to nodule formation except on hands

believed closely akin to infectious granulomas and were removed surgically or by electrodesiccation. Secondary atrophy was common at the site of former nodular lesions on the face, body, arms and legs, where it resembled but did not duplicate that described in lichen planus of the sclerotic-atrophic type. These lesions were not ivory white but contained much pigment (fig 1). On

slate to purplish brown to almost coal black. Splotches of dark pigment were common on the ears, around the eyes, on the lips, nose, neck and abdomen, in the axillas and groins, not infrequently on the gums and occasionally on the hard palate and the nail beds. Pigmented areas frequently were not at the site of earlier erythema or dermatitis, and

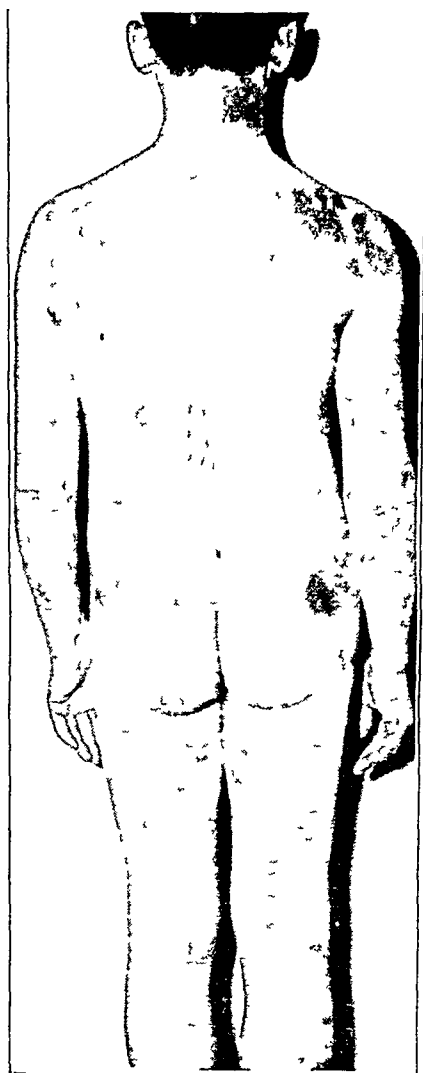


Fig 4—Generalized symmetric eruption, same patient as in figure 2, showing hyperkeratosis and extreme melanin pigmentation of neck and shoulders

dermatitis did not always develop at the site of the pigmentation. In 2 cases the ears were almost coal black, 1 of these was contracted in New Guinea and 1 in Italy. In both, the pigmentation definitely diminished during the period of observation but it was still decided when last observed (fig 4).

It was believed that all hyperpigmentation would eventually disappear. No treatment, except time, was of value.

The following observation was of interest. One medical officer had extensive vitiligo of both lower lids, dorsa of the hands, scrotum, feet and legs prior to entrance on active duty. While in Hawaii, with prolonged exposure to the sun, he had no eruption except slight erythema with some pruritus on the dorsa of the hands and the expected "tanning" of his normal skin. Within one week after his arrival in New Guinea, after he had taken quinacrine hydrochloride en route, a severe pruritus with



Fig. 5—Patient from Mediterranean Theater, showing hyperpigmentation and eczematization in same area. Note pigmented macules on neck.

some papular elements developed on the dorsa of his hands following exposure to sunlight. He then wore gloves, and one week later a pruritic erythematopapular eruption developed on his shins which had not been exposed to the sun in New Guinea. A few days later other portions of the body became involved, and he noted patches of purplish black pigmentation in the tanned areas on the face, ears, lips, neck, arms and legs. When he came under observation at this hospital two months later, he presented an erythematopapulonodular eruption which involved

the yellow-tinted skin and the vitiliginous skin to about the same degree. The eruption of the vitiliginous skin was brightly erythematous only, while that of the normally pigmented skin presented also purplish brown pigmentation. It was concluded that the pigment originated

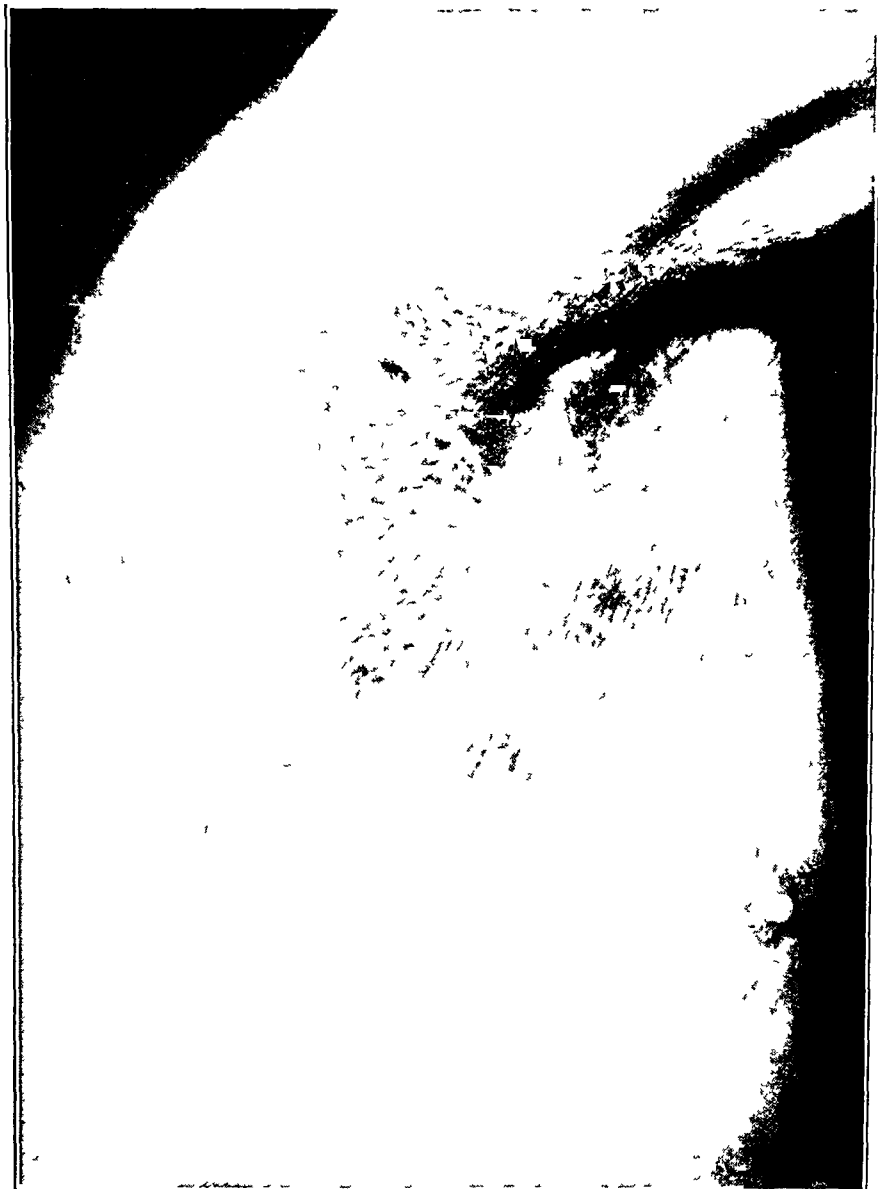


Fig. 6—Hyperpigmentation and eczematization in the same region, patient from New Guinea. Note resolving hyperpigmented lesions on chest and in axilla.

locally in the skin and was due to some unknown factor, probably of hematogenous origin, which stimulated the normal pigment-forming mechanism. This factor was not sunlight, because the legs had not

been exposed to sunlight in New Guinea. Because this pigment takes the Becker stain, which is considered specific for melanin, the pigment is undoubtedly melanin.

*Exudative Type* The exudative type more often began as an indefinitely outlined pruritic, erythematovesicular, patchy eruption on the fingers, on the dorsa of the hands or feet or in intertriginous areas. Not a few were diagnosed by the first medical officers to see them as dermatitis venenata, dermatophytosis or tinea cruris. The vesicles soon ruptured and became infected. Rapid extension of the eruption took place in some, while in others it remained relatively stationary for a time, only to "explode" suddenly and become generalized or even universal within a few days. Exudation was usually patchy but was often generalized. Many patients with eczematous lesions exhibited also patches of hyperpigmentation in the same areas (figs 5 and 6).

Crusts may be few or many and often cover pus-exuding lesions. In several cases of long-standing eruptions vegetating lesions developed.

Several patients with eczematous lesions only had lichen-planus-like lesions of the oral mucous membrane. In approximately 6 per cent of my cases there developed generalized to universal exudative dermatitis with profuse exfoliation (fig 7).

#### FACTORS IN ETIOLOGY

It is impossible at the present time to evaluate a number of observations. I have observed the disease in 1 Japanese, several Indians and approximately 300 white persons of various nationalities and ancestry but in no Negroes. Both types have been observed in blonds and brunets. The nodular type was relatively more common in blonds.

Dermatologists have long observed that exudative eczema, impetigo and infectious eczematoid dermatitis tend to become exacerbated and that contact dermatitis from either plants or drugs is more likely to develop on hot humid days. Appetite lessens, and loss of weight is the rule during hot summer months. All but a few cases of this disease to date have come from the New Guinea region which lies between 10 S and 10 N latitude. Temperatures at sea level seldom rise above 95 F and rarely fall below 70 F. The average relative humidity at five coastal stations throughout the territory over a five year period is 81 per cent at 9 a m, 75 per cent at 8 p m and 88 per cent at 9 p m<sup>1</sup>. Most patients stated that after a few weeks they "lost their appetite" and often discarded part of their food. Most of them had lost 10 to 50 pounds (4.5 to 22 Kg) in weight, although a few had not. Recent evacuees lost less weight than those returned several months ago.

There is no relation of the disease to combat, and some of the severest eruptions occurred in Service Force troops at fixed bases.

1 Challis, B. G. Climatic Notes on New Guinea, New Guinea Agric Gaz, December 1939.

Hygiene is probably a factor in determining the rapidity with which infection develops.

It has been repeatedly observed that the skins of these patients are easily infected and are easily irritated by medicaments which the skins of patients in the midwest section of the United States usually



Fig 7—Exudative exfoliation in a case of universal dermatitis. Patient had typical hyperpigmented nodular lesions on the chest. He was an American-Italian soldier from New Guinea.

tolerate well. Many eruptions promptly become exudative when the weather becomes hot and humid for even a few hours. It must be concluded that something has happened to these skins which renders them more vulnerable to both infection and irritation.

Several authors have described phrynoderma and hyperpigmentation with lichenification following the ingestion of diets deficient in vitamin A with improvement following large doses of that vitamin over long periods. In many of the cases cited here the patients were on C and K rations but did not eat all the ration. A complete C ration contains 9,450 U S P units of vitamin A, and K ration contains 4,674 U S P units. The minimum daily requirement of a 70 kilogram man on moderate activity is 3,000 U S P. units, and the recommended daily allowance is 5,000 units<sup>2</sup>. As far as I know, the requirement for persons at hard labor in a hot humid climate has not been determined. Vitamin A is known to be unstable, especially at high temperature. It is usually conceded that there is wide variation in the ability of different persons to utilize vitamin A, although most writers believe that huge amounts of the vitamin can be stored in the body provided there is adequate intake. The ability to absorb vitamin A is greatly diminished when diarrhea is present, and many soldiers in the New Guinea Area had diarrhea from various causes. Some authors contend that the entirely adequate diet should contain a safety factor of 100 per cent<sup>2</sup>. It is readily understood that much more investigation is necessary before definite statements can be made regarding the role of vitamin A as a predisposing factor in the disease discussed in this paper.

Most of the patients from both theaters had no fresh milk and little fresh fruits or vegetables for prolonged periods. On the other hand, many patients were given supplemental vitamins, especially vitamin A, some in large doses, without benefit. In this regard, it is recalled that McCollum in 1917 pointed out that in rats on diets deficient in vitamin A there developed severe spontaneous infections of the skin. However, this has not been proved to apply to man.

Almost all the patients in this series had mild to severe anemia. The whole problem of the porphyrins with regard to this disease needs investigation and promises to be worth while. Cultures have been negative for bacteria and virus. Few bacteria have been demonstrated in the biopsy sections and then only in the epidermis.

Insecticides are being studied by some investigators as the cause of certain cases of aplastic anemia and polyneuritis. While all the patients in this series had been exposed to insecticides, I currently believe that these materials play little or no part in producing the disease described in this paper.

Observations regarding quinacrine hydrochloride will be discussed later.

<sup>2</sup> Food and Drugs Federal Register (No. 227) 6 5922-5925 (Nov. 22) 1941, title 21, cited in *Inadequate Diets and Nutritional Deficiencies in the United States* Bulletin 109, National Research Council Washington D. C., November 1943 p. 3



## PATHOLOGY

In addition to the anemia, most patients also have an elevation of circulating eosinophils from 3 to 35 per cent. Sections of tissue usually contain an increased number of eosinophils.

The microscopic picture varies, depending on whether the eruption is "dry" or "exudative." The most decided changes are found in the dry type, which presents mild to severe hyperkeratosis and varying degrees of acanthosis. Some lesions exhibit decided pseudoepitheliomatous hyperplasia (fig 8 *A*). The hyperkeratosis tends to involve the entire length of the hair follicle and is often surrounded by perifollicular cellular infiltrate (fig 8 *B*). Some spongiosis is present in the basal cell and prickle cell layers. Clear cells are common in the malpighian layer, and in some areas the basal cell membrane is indistinct (fig 9 *A*). An increase of melanin in the basal cell layer is a constant feature and is patchy in type, varying from mild to intense and not always at the site of the underlying infiltrate. Dendritic cells and basal cells are often loaded with pigment (figs 9 *B* and 10 *A*), some of which may continue outward through the stratum corneum (figs 9 *B* and 10 *A*). The basal cell layer in some areas shows little increase of pigment, which seems to have "shaken out" and appears in clumps in chromatophores in the cutis where it tends to immobilize, especially in the tips of the papillae (figs 9 *B* and 10 *A*). Pigmentation is less intense in areas where acanthosis and pseudoepitheliomatous hyperplasia are more evident (fig 8 *A*). Some sections present a classic picture of "lichen planus" (fig 10 *B*). All sections demonstrate atrophy to absence of sebaceous glands, although the erector muscles are often retained. Atrophy of the hair follicle is demonstrated in some cases. Sweat glands may be unaffected or surrounded by infiltrate, and some atrophy may occur. Secondary eczematous changes may be present in varying degrees, with eosinophilic infiltrate, but even in these cases the hyperkeratosis and the atrophy of the sebaceous glands are retained. The end stage is characterized by increased pigmentation, thinning of the rete ridges and atrophy of the dermal appendages. I believe that some of the atrophic appendages later regenerate. No attempt was made to prove this contention by second biopsies, and the belief is based on clinical observation alone.

## CLINICAL COURSE

Some observers in the New Guinea Area and I have seen numerous complications, including universal exfoliative dermatitis, hepatitis, atypical pneumonia, polyneuritis, heart bundle-branch block, pericarditis, ascites, a low level of total protein in the blood, reversal of the albumin-globulin ratio, edema and anasarca, simple anemia and aplastic anemia. In 2 patients of this series there developed pulmonary tuberculosis.

Simple anemia is common in both types of the disease. Exfoliative dermatitis was observed in both types. Atypical pneumonia occurred in 2 patients with exudative eruptions at this hospital. I have



Fig 8—A, biopsy specimen showing verrucous lesion with decided acanthosis and pseudocarcinomatous hyperplasia. Hematoxylin and eosin  $\times 30$ . B, keratotic plugging of follicles and perifollicular hyperplasia greatest at depth of follicles but with some atrophy of follicular walls. Hematoxylin and eosin  $\times 48$ .

observed 4 patients with paresthesia of the extremities, 2 of whom exhibited muscular incoordination in all four extremities. All 4 had an increased amount of globulin in the spinal fluid and an elevated

level of total protein, between 105 and 175 mg per hundred cubic centimeters, without other changes. The eruptions of all 4 were "dry." Several patients with aplastic anemia in conjunction with this dermatosis were observed in the Southwest Pacific Area, and 2, of whom 1 died,



Fig 9—*A*, hyperkeratosis, thickening of granular cell and prickle cell layers, narrowing of rete pegs, some liquefaction of basal cell layer and intense cellular exudate in papillary and subpapillary layers consisting principally of histiocytes and lymphocytes. Hematoxylin and eosin  $\times 85$ . *B*, acanthotic process with increase in granular layer. Numerous dendritic cells laden with melanin pigment and pigment-laden chromatophores in the cutis. Silver nitrate and hematoxylin  $\times 155$ .

have been seen at this hospital. In both the eruptions were of the "dry" type. Heart bundle-branch block was observed in 2 patients with dry dermatitis. Ascites occurred in 2, the eruption of the one being dry and of the other exudative. Low levels of total protein in the blood



Fig 10—*A*, section from patient with disease resembling Richl's melanosis showing keratotic plugging of sweat duct and tremendous increase in pigment in small area involving basal, dendritic and clear cells and extending up into stratum corneum and down into chromatophores in the cutis. Silver nitrate and hematoxylin  $\times 115$ . *B*, typical picture of "lichen planus" with hyperkeratosis, increase in granular layer, liquefaction degeneration in basal cell layer and cellular infiltrate limited to upper portion of cutis. Section also showed atrophy of hair follicles dilatation of sweat glands and definite increase in melanin pigment. Hematoxylin and eosin  $\times 85$ .

are common in patients with severe exudative eruptions, while a reversal of the albumin-globulin ratio with edema was observed in 4 and anasarca in 1

I do not desire to give the impression that all these conditions, especially atypical pneumonia, polyneuritis and heart bundle-branch block are proved to be due to the disease entity or that they are due to the same etiologic factors. However, they did occur as complications. Major Clarence Livingood has seen numerous diphtheritic infections secondary to the disease under discussion, especially the eczematous type, and has encountered both polyneuritis and heart bundle-branch block in some of his cases. Although it is possible that the 6 patients reported on in this paper had had diphtheritic infections there was no note in the clinical record to this effect, and the patients gave no history of having had open lesions. It is, therefore, believed that both these conditions are probably unusual manifestations of the disease itself.

#### OBSERVATIONS REGARDING THERAPY

Vitamin A was given in 100,000 U S P unit doses daily for three weeks to a small group of patients with eruptions of both types, with no evident benefit. It is realized that the period of observation was short. A high protein, high carbohydrate, low fat diet (modified Varco diet) was given to a group of patients with exudative lesions for two weeks, with no definite effect. Supplemental feedings of Dietene were given to some patients and were believed to be of some benefit in that the gain of weight was more rapid. Intramuscular injections of bismuth subsalicylate were given to several patients with nodular eruptions. No definite benefit was noted. Injections of mercurial preparations were not tried. One observer overseas noted generalized exudative dermatitis following intravenous administration of oxophenarsine hydrochloride (mapharsen). I gave solution of potassium arsenite U S P, in ascending doses, beginning with 2 minims (0.12 cc) three times a day and increasing by 1 minim (0.06 cc) a day, to 4 patients with nodular eruptions, with 100 per cent poor results, manifested within two weeks by increased pruritus, oozing dermatitis, edema of the lower extremities and albumin, red blood cells and granular casts in the urine. The drug was promptly discontinued.

Mild and severe pyoderma universally responded well to penicillin intramuscularly in 20,000 to 50,000 unit doses every three hours for a total of 200,000 to 1,000,000 units. Local applications of penicillin in wet dressings seldom controlled the infection and frequently produced dermatitis when used in concentration of 250 units per cubic centimeter. Five per cent sulfadiazine ointment occasionally gave good results in cases of mild and localized eruptions but frequently produced exacerbations.

Wet packs of solution of boric acid constantly for three to ten days in the cases of acute eczematous eruptions was the most satisfactory, although several failures were noted. Some of these failures responded to solution of potassium permanganate (1:10,000) applied in wet dressings and some to 0.12 per cent silver nitrate solution packs. Solution of aluminum acetate and alibour water (water containing zinc and copper sulfates) in proper dilutions gave satisfactory results in a few cases but often failed. Few patients in my experience tolerated boric acid ointment, for some reason yet unknown. Twenty per cent zinc oxide in Aquaphor (an oxycholesterol-petiolatum ointment base) was usually well tolerated after boric acid packs were discontinued. Three to 5 per cent ammoniated mercury in Aquaphor base was helpful in some cases.

For eczematous eruptions with vegetating lesions and for those with infiltrated pyogenic lesions roentgen irradiation in doses of 100 r weekly for four or five weeks proved most beneficial. Chronic exudative patches also usually responded after one to four irradiations.

Blood plasma and concentrated human serum albumin daily proved helpful in cases of extensive eczematous eruptions with low total protein in the blood and especially in those with reversal of the albumin-globulin ratio. It is desired to caution against the use of plasma in cases in which it is not needed because of the possibility of plasma or infectious hepatitis and jaundice three or four months later.

*Relation to Malaria and Quinine* Some of the patients had malaria overseas and in this hospital. Some had their first attack in the hospital. A few had no malaria. In 1 patient aplastic anemia developed two weeks after treatment of an attack of malaria with quinacrine hydrochloride. During the period of anemia, the patient had several slight chills with fever, but blood smears were consistently negative for plasmodia. After several transfusions, a sternal puncture was done. Many malarial parasites were demonstrated in the marrow smear. After this observation, several patients without known malaria were given quinine as in the treatment of malaria, and the dermatitis was not affected.

*Quinacrine Hydrochloride and Dermatitis* Several patients had two to four attacks of malaria in this hospital. The first attacks were treated with quinacrine hydrochloride. In none of the cases did the dermatitis improve during the period of treatment. Three patients with dry lesions and involvement of the mucous membrane manifested increased soreness of the tongue and increased prominence of the lesions. In 1 patient with dry lesions severe exfoliative dermatitis developed on the fourth day of treatment. In several there developed increased pruritus with slight oozing in the groins. Several eczematous eruptions became

more exudative. Subsequent attacks were treated with quinine. A few patients manifested slight exacerbations of the dermatitis with the second attack of malaria which was treated with quinine. None had exacerbations with subsequent attacks which were treated with quinine, and several actually improved during the period of treatment. Three patients with previous exacerbations of their lesions during an attack of malaria treated with quinacrine hydrochloride were then given quinacrine as in the treatment schedule. There were exacerbations of the lesions of 2 in two days and of those of 1 in four. Two patients with patchy eczematous lesions, which had been dry for two and three weeks, respectively, and who had been receiving suppressive therapy with quinine, were given 0.65 Gm of quinacrine hydrochloride daily. In the one increased pruritus and oozing developed on the fourth day and in the other on the ninth.

It is worthy of note that not all the eczematous eruptions became aggravated when the drug was being taken. Patients with dry nodular lesions almost universally noted increased pruritus, increased infiltration and more elevation of the nodules after taking daily doses of 0.3 or 0.65 Gm of the drug for two to four weeks and some in much less time.

*Quinacrine Hydrochloride and Quinine as Suppressive Agents*—Observations at this hospital agreed with those at others in that quinacrine hydrochloride proved a more efficient suppressive agent than quinine.

*Patch Tests*—Test patches with quinacrine hydrochloride being used in Aquaphor base in dilutions of 1:1,000, 1:200, 1:100 and 1:10 were applied to the normal-appearing skin of 7 patients, 4 with eczematous eruptions and 3 with the dry type, as well as to 4 controls who had never taken quinacrine hydrochloride. All tests elicited negative reactions after seventy-two hours, except that of 1 patient with a generalized dry patchy follicular eruption (shown in figure 1) from the Mediterranean Area, who exhibited rather intense erythema with a moderate papulovesicular dermatitis at the site of the patch which covered a few maculopapular lesions. Aquaphor containing 1 per cent quinacrine hydrochloride was applied to small patches of skin of 3 patients with universal dermatitis which had become subacute. In all 3 acute vesicular dermatitis developed under the patch within twenty-four hours. In 2 of these there developed an exacerbation of the generalized dermatitis. Two patients with localized patches of dry dermatitis which had previously become exudative after the drug had been taken by mouth and whose normal skin did not react to test patches with 1:10 quinacrine hydrochloride ointment applied 1:100 ointment to small areas within the patches every three hours for three days. On the third day, each had a vesicular eruption in the patch where the ointment was applied. A

vesicle occurred at each follicular opening, and there was little inter-vesicular erythema. Other patients were then tested, and with only one exception all the tests elicited the same reaction. Eczematous lesions in soldiers who had never taken the drug did not give this reaction. It was thus concluded that only that skin on which there had previously been an eruption was reactive.

#### COMMENT

From the foregoing observations, I am convinced that quinacrine plays the major part in the causation of this new disease entity. Whether it is the entire cause must be left to further investigation.

The observation of one investigator overseas and of myself that arsenic, either oxophenarsine hydrochloride or solution of potassium arsenite U. S. P., produces very adverse effects is interesting. It is worthy of note that practically all the manifestations of this new disease have been observed following arsenical medication.<sup>3</sup> Symptoms of chronic arsenical poisoning are usually given about as Davison<sup>4</sup> gave them. Weakness, anorexia and jaundice may be present and often low fever, "overgrowth of horny layer, especially palms and soles. Frequently there appears an arsenic melanosis. Anemia is a common result of prolonged use of arsenic. Multiple neuritis may occur, this generally involves the limbs rather than the trunk. Paralysis of sensation followed by motor paralysis is not uncommon." Feinberg<sup>5</sup> wrote "We are forced to regard these manifestations as reactions due to allergy. Among such common effects of hypersensitivity are dermatitic rashes of various types, urticarial eruptions, fixed drug eruptions, exfoliative dermatitis, hepatitis and other types of liver damage, hemorrhagic brain lesions, hematopoietic disturbances including aplastic anemia, granulocytopenia and thrombocytopenia, asthma and rhinitis and anaphylactic shock. The specificity of these reactions varies in different persons. In some it extends to practically all arsenicals, although in a larger number the benzol radical is the active part of the antigen." It is interesting that both the arsphenamines and the quinacrine hydrochloride contain benzyl radicals. The same author stated, "The status of skin tests in arsphenamine allergy is uncertain. It is true that patch reactions are often obtained, but such reactions are frequently present in those who show no clinical allergy and are often absent in those who display frank allergic symptoms." He also cited experiences of Sulzberger and Simon.

3 Sulzberger, M. B. *Dermatologic Allergy*, Springfield, Ill., Charles C. Thomas, Publisher, 1940, p. 294.

4 Davison, F. R. *Synopsis of Materia Medica, Toxicology and Pharmacology*, ed. 2, St. Louis, C. V. Mosby Company, 1944, p. 535.

5 Feinberg, S. M. *Allergy in Practice*, Chicago, The Year Book Publishers, Inc., 1944, p. 343.



with sensitiveness to arsphenamine in guinea pigs, which could be sensitized in some cities but not in New York. The effect of the climate per se on allergy is not understood.

Just how long quinacrine can be retained within the human body is not yet known, although Kehar, working with monkeys, has reported elimination prolonged up to fifty-one days and others have reported retention for as long as sixty-nine days.

One of the tests for quinacrine is its yellowish green fluorescence under ultraviolet rays in solutions up to 1:5,000,000 dilution. A section of liver from 1 patient in this series, who died of aplastic anemia, gave a brilliant fluorescence after one month's immersion in solution of formaldehyde. The patient had taken no quinacrine hydrochloride for two months.

#### SUMMARY AND CONCLUSION

A protean disease with symptoms which are mainly dermatologic but with numerous somatic manifestations, occurring with great frequency in the New Guinea Area and with much less frequency in the Mediterranean Theater, is described.

The cause is not known, although several factors are probably involved, including low vitamin intake, especially vitamin A, quinacrine hydrochloride (atabrine) and allergy. It is believed that vitamin A deficiency predisposes to the disease but that quinacrine hydrochloride is the major factor.

The symptomatology and classification are given.

The pathologic changes are described and illustrated.

The importance of this disease is expected to diminish rapidly as large concentrations of troops are moved from New Guinea and Southern Italy.

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## NEURODERMATITIC REACTION

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BY NEURODERMATITIC reaction we mean a pathologic process, and not a disease. The term is used because the microscopic changes in this process are similar to those found in the disease neurodermatitis. The reaction is characteristic of such dermatoses as neurodermatitis, nummular eczema and exudative lichenoid and discoid chronic dermatosis.

It is often difficult clinically to diagnose these dermatoses and to differentiate others from them. A microscopic diagnosis would be of considerable assistance but unfortunately this is not always conclusive. The subject is of sufficient importance to stimulate further study. This presentation may suggest a somewhat different point of view as a basis for new investigations.

The neurodermatitic reaction involves both the cutis and the epidermis. The latter is usually acanthotic and shows some degree of regularity, there is, as a rule, little evidence of edema. A focal infiltration composed of small round and wandering connective tissue cells is found about the vessels of the middle and the upper layer of the cutis and the walls of the arterioles and small arteries are thickened. These findings are not constant and the differential diagnosis depends on these variations.

We offer the following outline which includes not only the dermatoses characterized by the neurodermatitic reaction but also indicates the diseases from which they must be differentiated.

### THE NEURODERMATITIC REACTION

#### I Neurodermatitis

A Neurodermatitis disseminata

B Neurodermatitis circumscripta (lichen chronicus simplex of Vidal)

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University, New York

- II Nummular eczema     $\left\{ \begin{array}{l} \text{with edematous vesicle} \\ \text{with cellular vesicle} \end{array} \right.$ 
  - A So-called pustular psoriasis
  - B Pompholyx
    - 1 Type due to increase and retention of sweat
    - 2 Type due to fungous infection
  - C Dermatitis venenata (contact dermatitis)
    - 1 with edematous vesicle
    - 2 with cellular vesicle
- III Exudative lichenoid and discoid chronic dermatosis
  - A Iodide or bromide eruption
  - B Lymphatic leukemia
  - C Mucosis fungoides

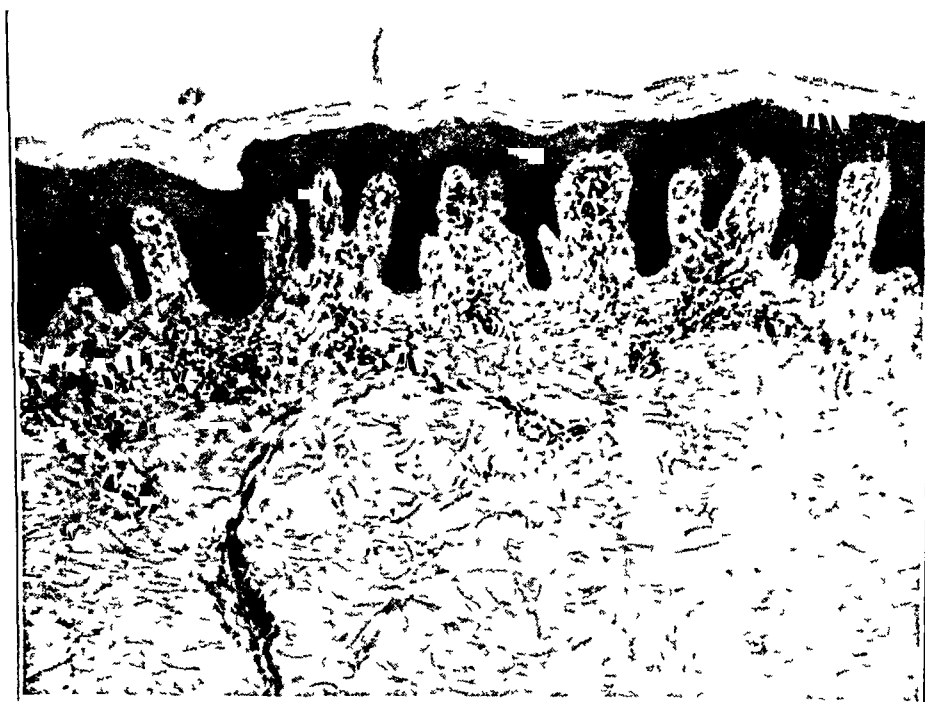


Fig 1—Neurodermatitis disseminata. Note regular acanthosis and focal cellular infiltration about the vessels of the middle and upper layers of the cutis.  $\times 88$

#### NEURODERMATITIS

The clinical picture of neurodermatitis needs no comment. The pathologic process involves both the epidermis and the cutis. The former is dry and, although the intercellular spaces may be accentuated, the basal cell margin is unaltered; the granular and horny layers are present and may be increased, and a rather regular acanthosis is usually present. However, friction, scratching, medication, etc., may super-

impose a traumatic dermatitis. This would account for the presence of an irregular acanthosis, edema and even parakeratosis. We feel that these are evidences of secondary eczematization and not part of the disease itself.

The small vessels of the middle and upper layers of the cutis are dilated and their walls thickened. About them is a focal infiltration of small round and wandering connective tissue cells, there are no plasma, epithelioid or giant cells. Throughout the area is moderate interstitial edema; the papillary bodies are not exaggerated, the elastic tissue is unchanged, but, where the cellular infiltration is pronounced, it may be pushed aside.

There are clinical differences between lichen chronicus simplex and neurodermatitis disseminata, but both present the microscopic picture which has been described. Therefore the pathologic findings cannot establish a final diagnosis unless they take into consideration the clinical features.

#### NUMMULAR ECZEMA

Nummular eczema occurs in various-sized discoid or oval patches. It is found on the dorsal surface of the hands, the fingers and the forearms, it also appears on the extensor surfaces of the thighs and the legs. Although both the upper and the lower extremities may be involved, there is no symmetry. Each lesion is an inflammatory erythematous patch containing grouped vesicles. The size of these patches varies from that of a dime to that of a quarter or larger. The vesicles persist until they finally break and form crusts. Severe itching is constantly present. The patches appear suddenly and spread peripherally; occasionally they undergo involution in the center, leaving a brownish discoloration; however, no atrophy or scarring results. In time new lesions appear on the same, or new, locations.

Although this is the usual clinical picture, other manifestations are frequently seen. Lesions may appear anywhere; patches may be large or smaller ones may fuse together and cover a considerable surface of the skin. Vesicles and crusts may be absent, and there may be only an erythematous, scaly area. Thus, the disease may simulate eczematized neurodermatitis, contact dermatitis, seborrheic dermatitis, dermatophytosis, dermatophytid, dermatitis herpetiformis and other varieties of eczema.

The pathologic features of nummular eczema differ from those of neurodermatitis only by the presence of an intraepidermic cavity. When the process has dried or even in a well developed lesion in which the vesicle is missed the features are identical. However, in a typical picture this epidermic cavity is the differential feature. There may be one or more vesicles; these may be large or small and contain fluid.

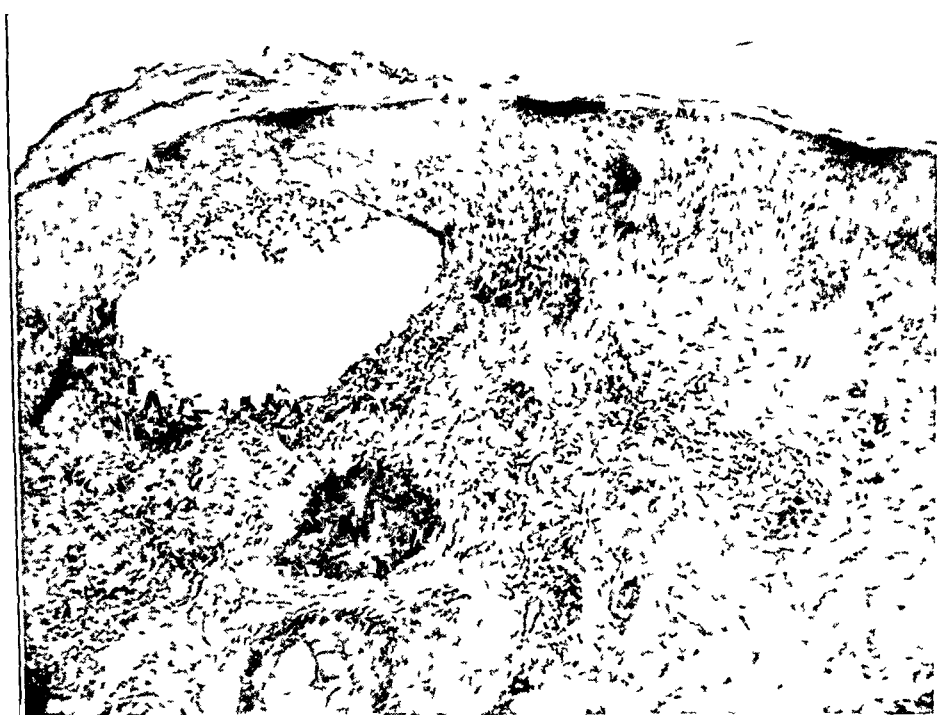


Fig 2—Nummular eczema Note the edematous type of vesicle in the epidermis and focal cellular infiltration about the vessels  $\times 88$

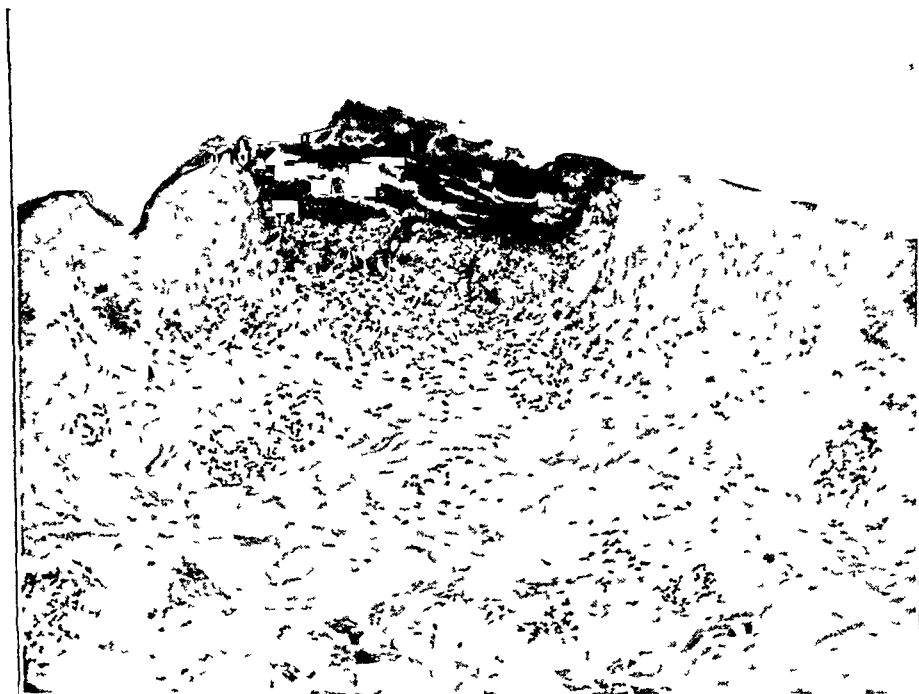


Fig 3—Nummular eczema Note the cellular type of vesicle, regular acanthosis and focal cellular infiltration about the vessels  $\times 88$

cells or both. There is little or no edema about the vesicle and this differentiates it from eczema. The remaining findings are those described under neurodermatitis.

However, similar vesicles are seen in other diseases. First so-called pustular psoriasis is characterized by this type of vesicle but within it are numerous polymorphonuclear leukocytes, many of them broken down. In other words it is a true pustule. The more important distinguishing features are to be seen in the cutis. There is a mild inflammatory reaction in the subepidermic region but this is chiefly in the area of the pustule, and the vessel walls are not involved.

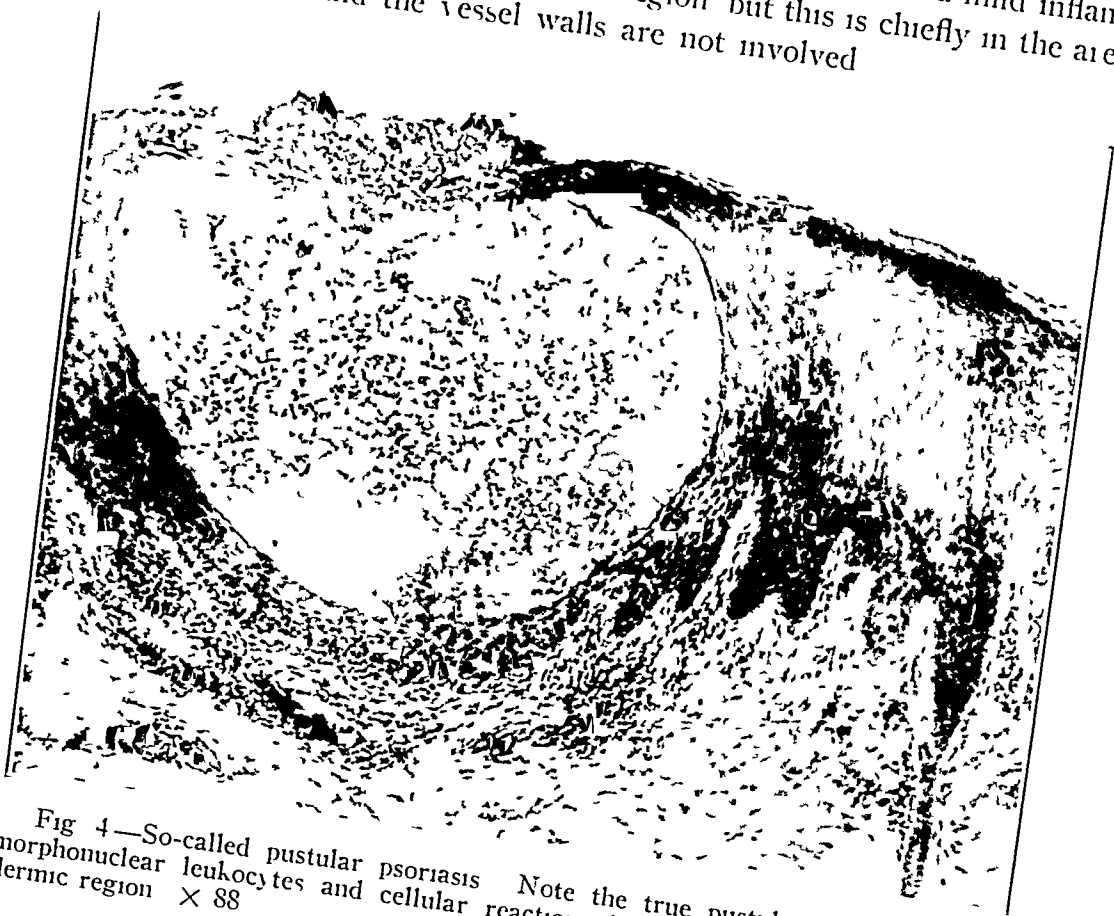


Fig 4—So-called pustular psoriasis. Note the true pustule containing polymorphonuclear leukocytes and cellular reaction about the vessels in the subepidermic region.  $\times 88$

So-called pustular psoriasis is different from psoriasis with pustules. In the latter one finds all the features of psoriasis, and the pustule is secondary, small and high in the epidermis. In so-called pustular psoriasis the pustule is large primary and may extend throughout most of the epidermis.

The second disease to be differentiated from nummular eczema is pompholyx. There are two types, one due to increase and retention of sweat and the other due directly, or indirectly, to a fungous infection. In the first, the vesicle contains only fluid, and at its base the opening of a sweat duct is visible. Thus it appears that this vesicle is due

primarily to some physiologic rather than pathologic, process. It is true that the vesicle of the other variety of pompholyx also contains only fluid, but a sweat opening is not found. At times, a fungus can



Fig 5—Psoriasis with pustules. Note typical picture of psoriasis with secondary pustulation.  $\times 114$

be demonstrated. There is a mild diffuse inflammatory process in the upper cutis and subepidermic zone and plasma cells may be present.

Finally, contact dermatitis should be considered with this group. The vesicles are usually small, numerous and at the surface of the

epidermis. They are filled with fluid cells or both. The cells are identical with those of the underlying inflammatory process which is composed of small round and wandering connective tissue cells. The primary irritant type of contact dermatitis may have pustules not only in the epidermis but also in the cutis directly beneath the epidermis and especially about the hair follicles and sweat ducts. The epidermis is not acanthotic.

EXUDATIVE LICHENOID AND DISCOID CHRONIC DERMATITIS  
In its different stages exudative lichenoid and discoïd chronic dermatitis clinically may closely resemble pityriasis rosea eczema contact

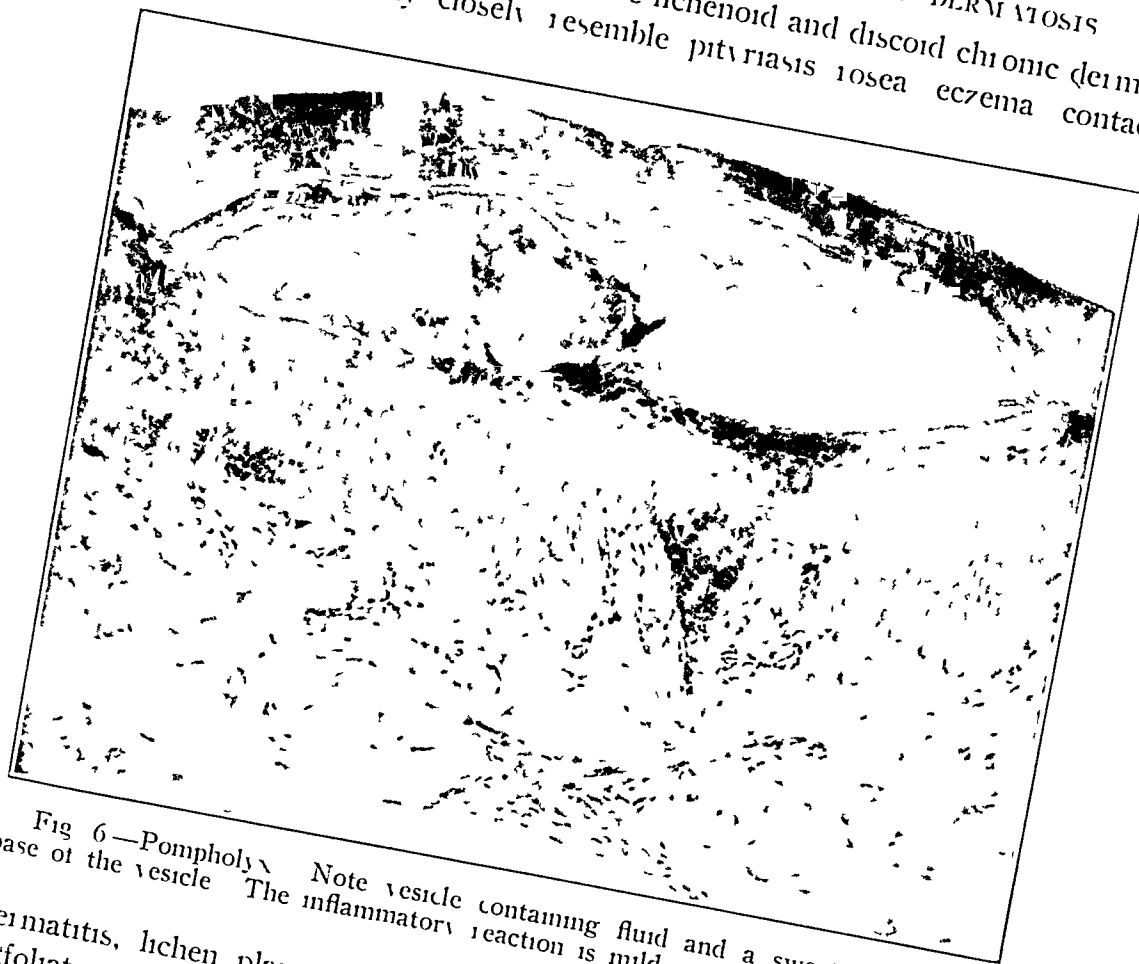


Fig 6—Pompholyx. Note vesicle containing fluid and a sweat duct at the base of the vesicle. The inflammatory reaction is mild and diffuse.  $\times 88$

dermatitis, lichen planus dermatitis herpetiformis mycosis fungoides exfoliative dermatitis etc. The lesions and the entire general picture change from one phase to the other. However the many clinical variations may be explained by the intensity of the reaction, for the basic pathologic findings are fairly constant and conform to those of the neurodermatitic reaction. Although acanthosis may be slight usually it is pronounced. In some stages edema may be slight while in other phases it will be extensive showing all gradations from basal cell disturbance to parakeratosis. Small super-



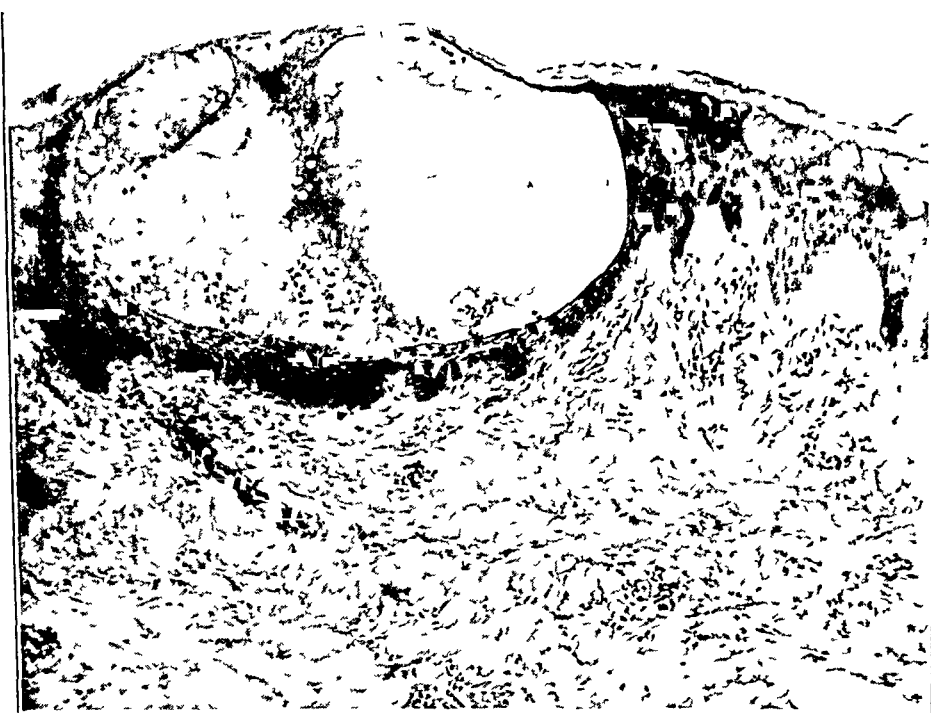


Fig 7—Contact dermatitis. Note the edematous type of vesicle containing a few cells that are identical with those of the underlying simple type of inflammatory reaction  $\times 88$



Fig 8—Contact dermatitis. Note the cellular type of vesicle. The inflammatory reaction is composed of small round and wandering connective tissue cells  $\times 88$

ficial vesicles simulating contact dermatitis may be present. The latter can be, and in fact often are superimposed. When edema not in the sense of eczematization, but of primary nature and part of the process is found in the epidermis it is important as a distinguishing feature of this group. However, the most striking feature of exudative lichenoid and discoid chronic dermatosis is the presence of plasma cells in the focal cellular infiltration which are found close to the vessel wall. Only an occasional epithelioid cell may be seen.



Fig 9—Exudative lichenoid and discoid chronic dermatosis. Note regular acanthosis and focal cellular infiltration about the vessels of the middle and upper layers of the cutis.  $\times 88$

From this last disease, iodide and bromide lesions must sometimes be differentiated. This is not easy or always possible. In the early stages the epidermis is not involved, and the infiltration is composed chiefly of polymorphonuclear leukocytes and small round cells that at times resemble lymphocytes; the vessel walls are not thickened. Later the cellular infiltration becomes extensive, there are many types of cells, liquefaction necrosis and finally, granulation tissue appear.

Lymphatic leukemia should also be considered here. Differentiation is rather simple as the epidermis is passive and the cellular infiltration is made up entirely of lymphocytes. These are of uniform size and round, but slightly larger than a small round cell and have a small

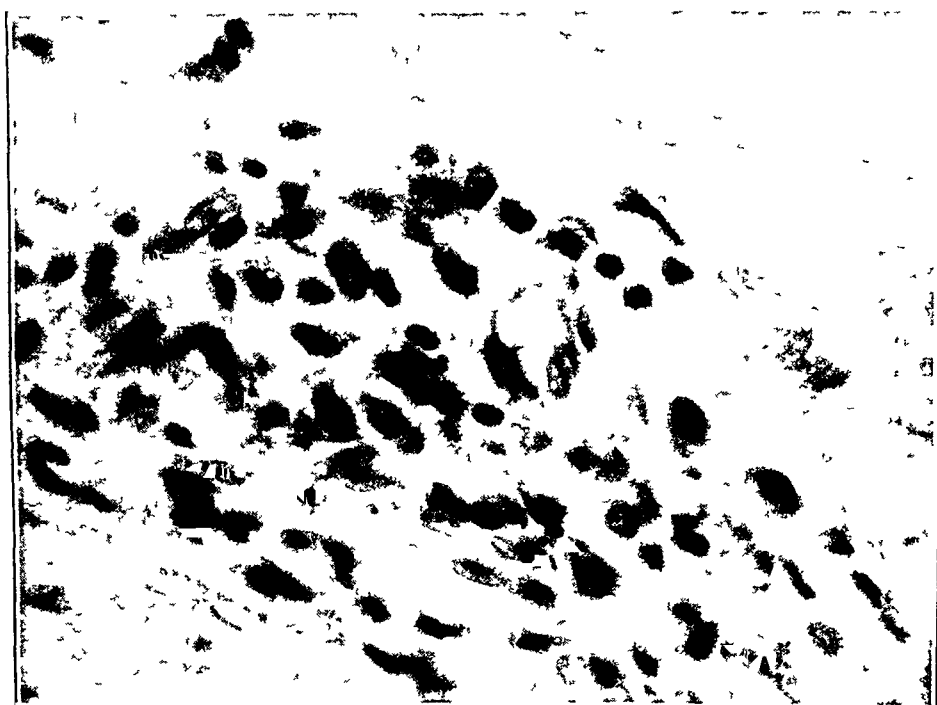


Fig 10—Exudative lichenoid and discoid chronic dermatosis. Note dilated vessels with thickened walls. Plasma, wandering connective tissue and round cells may be seen in the infiltration.  $\times 944$



Fig 11—Mycosis fungoides. Note an acanthotic epidermis and focal cellular infiltration about the vessels. A Pautrier abscess may be seen in the upper part of the epidermis.  $\times 116$

amount of cytoplasm about the nucleus. The nucleus is also round and the chromatin is not densely packed.

The last and probably the most important disease to be considered in this group is mycosis fungoides. One of the reactions seen in the early stage suggests exudative lichenoid and discoid chronic dermatosis. The epidermis may show no characteristic change, if Pautrier's abscess is present, it is diagnostic. In the cutis the infiltration is focal about the vessels and although other cells are present, the epithelioid cell predominates. In a well established lesion there are different types of cells, reticulum, grouping of the cells, breaking up of nuclear material, clumping of nuclei, mitotic figures and Pautrier's abscesses. When these other features of mycosis fungoides are present, they are of considerable aid in arriving at a diagnosis.

#### COMMENT

In both types of neurodermatitis there are the typical features described for the neurodermatitic reaction. Nummular eczema differs only in the presence of an intraepidermic vesicle. Exudative lichenoid and discoid chronic dermatosis is characterized by the type of cell in the focal inflammatory reaction. In the first two, the cellular infiltration is typical of an exudative inflammatory process, in the last group, it is of the productive variety. In all three the walls of the arterioles and the small arteries are involved.

Clinically, there is a close relationship between these dermatoses. Patches of nummular eczema are seen in cases of neurodermatitis, and exudative lichenoid and discoid chronic dermatosis may at times suggest either disseminated neurodermatitis or nummular eczema. Incidentally we believe that nummular eczema is of frequent occurrence, and that many more of the vesicular diseases of the extremities may belong in this group.

#### SUMMARY

A classification of the neurodermatitic reaction is presented. The dermatoses in this group may easily be confused, and only careful consideration of both the clinical and the microscopic features will establish a final diagnosis.

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## A STUDY ON ULCUS PHAGEDENICUM CUTIS

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ULCERS of various origin such as diphtheria leishmaniasis cutis and tropical ulcers are rather common in the countries of the Near East but in the years during which we have seen a number of them we have also frequently encountered a special type which does not fit into any of the aforementioned categories

Its distinction from the aforementioned ulcers is determined by its clinical aspect and by the bacterial flora it presents. In connection with the desert warfare in the Near East the problem has gained particular importance

To characterize the cases which we have seen during the last ten years it seems to us that the most appropriate term would be "phagedenic ulcer". This denotes a circumscribed inflammation of the skin which may lead to destruction of the entire cutis and subcutis down to the fascia, progressing in waves and on the whole running a chronic course, and occasionally new outbreaks being accompanied with reactions of a generalized nature. The ulcers do not tend to heal spontaneously

We collected data on 58 cases most of them in the last few years, a fact which may serve as an indication of the comparatively frequent incidence of the lesion in this and the neighboring countries. Thirty-three of the patients were admitted to our hospital while 25 remained outpatients. Since for the latter it was impossible to make all the various tests and laboratory examinations, as some of the patients called irregularly and some of them only once, they were included only insofar as the data were considered relevant. With regard to the 33 inpatients, various systematic examinations could be made. In order to avoid tedious case histories, the data are summarized and characteristic illustrations attached

In all our patients we found normal conditions with regard to the urine, feces, blood cell count, chemical analyses of the blood for urea, sodium chloride, glucose and in the majority of cases, calcium. Wassermann and Kahn reactions were invariably negative except for

From the Dermatologic Department of the Rothschild-Hadassah University Hospital, Head Dr. A. Dostrovsky

those of 1 patient in whom the tests elicited slightly positive reactions. In some patients the gastric juice could be analyzed, and determinations made of vitamin C in the blood and urine. In others roentgenograms of the lungs, experiments with animals (tuberculosis) could be made and blood sedimentation rate and basal metabolic rate could be determined. The results of these examinations showed wide variations and no constancy could be established.

#### DISCUSSION OF THE MATERIAL

*Clinical Appearance* The first sign of the beginning ulcer is a sanguineous pustule surrounded by a bluish red discoloration of the skin. When the upper part is removed one finds a greater degree of destruction in the depth than one would expect, judging by the outward appearance (fig 1). The edges are already slightly undermined.

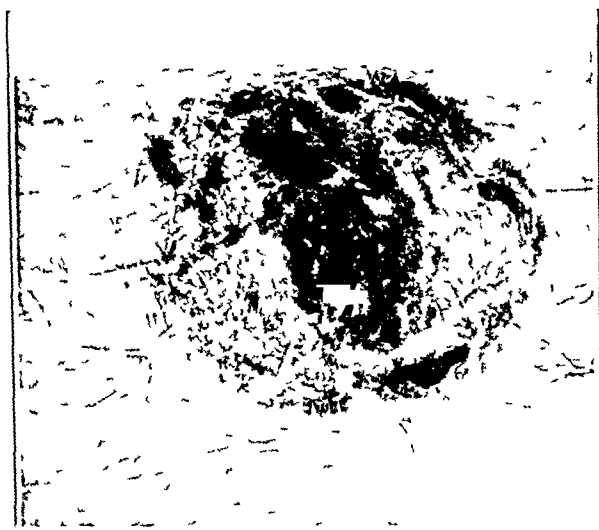


Fig 1—After removal of upper crust, a greater destruction in depth is shown than one would suspect.

In general patients are rarely seen in that stage, as they usually seek medical advice only when the process has already reached the stage of extensive ulceration. In our patients the ulcers were on an average 5 to 6 cm in diameter, some of them reaching a size of 15 to 20 cm. The floor was uneven with additional slight depressions, and covered with a serous, occasionally mucopurulent or gelatinous, secretion which had an offensive smell, reminding one of the smell of raw meat. No considerable discharge from the surface was noted. The color of the floor was gray, sometimes slightly sanguineous.

The bluish red edges were extensively undermined in typical cases the epidermis hanging down in curtain fashion, while below them the cutis as well as the subcutis had disappeared. This portion of the edge was found to be soft and brittle and of an even darker tinge.

Acute progression would occasionally occur by way of undermining corridors, in 1 case of 8 cm in length on an average however not exceeding 1 to 3 cm

After some time, these corridors would open into new ulcerations in such a way that here subsidiary ulcers were formed. More or less wide bridges of normal skin remained either not involved at all or only later becoming necrosed.

The skin surrounding the ulcers was inflamed and swollen. In a great number of cases, starting from a line exactly coinciding with the outer margin of the undermined portion the ulcers were surrounded by an area of superficial detachment of the epidermal layer.

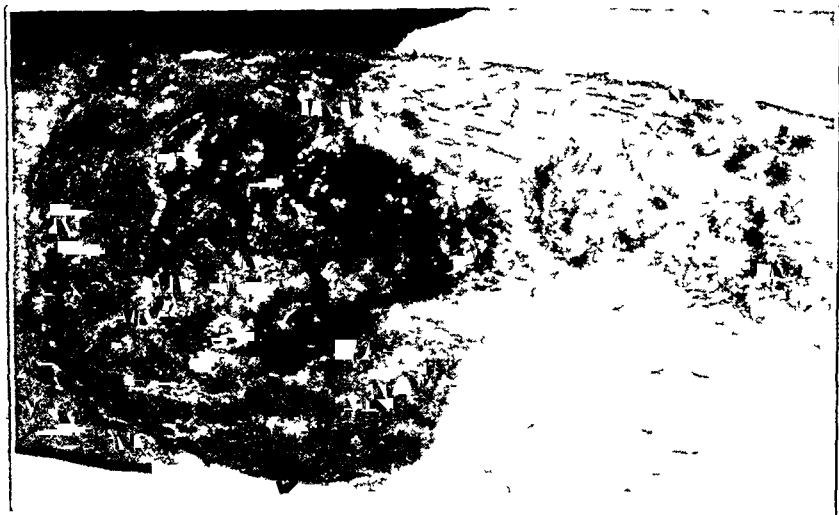


Fig 2—Lesion 15 cm in diameter, ulcer being only 3 cm in diameter

In 1 of the patients such an area of detachment was 15 cm in diameter while the ulcer itself occupied an area of only 3 cm in diameter. Reference to this peculiar feature has not been found anywhere in the literature, although in our opinion it should be considered as one of the characteristics of that lesion. It is not yet clearly understood whether maceration or secretion or the invasion of germs may account for this superficial epidermal detachment. The outer edges of these areas showed, as a matter of fact, something in the nature of undermining so that the original ulcer seemed to be reproduced in the shape of a superficial erosion.

As a rule the ulcers occur singly and only rarely are two or more observed in the same person simultaneously. In the literature, however, cases of extraordinary severity have been described, multiple ulcers being present all over the body.

*Location* As a general rule, the lesions may be expected to occur anywhere on the skin—that is, anywhere that trauma may affect the skin and invasion of germs may take place. In our cases we noted predilection of certain locations. In the following table the location of the ulcers in 51 cases is recorded.

In no case was the localization that of varicose ulcers, found as an accompaniment of enlarged veins. The malleolar ulcers were always immediately on the osseous surface, occasionally spreading from there.

Since the majority of the patients were young, varicose veins rarely came into the picture at all, hence, the circulatory factor could be safely eliminated. It appears to be of far greater significance that out of fifty-one ulcers forty-one were found on the malleoli and tibiae—on places where exposure to injury and pressure is particularly

TABLE 1—*Location of Ulcers in Fifty-One Cases*

Location	No. of Cases
Malleolus	17
Medial	12
Lateral	5
Tibia	24
Lower third	17
Upper portion	7
Upper extremities	4
Mamma (fig. 9)	2
Inguinal region	1
Iliac region	1
Femoral region	1
Gluteal region	1
Total	51

great. Location, therefore, seems to be one of the essential factors in the causation of the lesion.

As to complications, there was erysipelas twice and in 2 cases necrosis of the tendons of the superficial extensor surfaces of the foot and of the achilles tendon. In a postoperative ulcer of the chest there was perforation into the pulmonary tissue.

Three of our patients died, 1 from pyopneumothorax and 2 after operative treatment of the ulcers in Europe and the United States of America, respectively.

*Age* The age distribution is given in table 2, showing a fair share of all age groups.

Out of 58 cases therefore in 48 the patients were under 40 years of age. The maximum frequency is found between 15 and 40. It should, however, be borne in mind that the age distribution of Palestinian Jews is an abnormal one in view of recent immigration with prevalence of the younger groups. Immigrants were by the way, found to be attacked by the disease in the same way as natives.



*Sex*—Males outnumbered females by 30 to 28, a prevalence of the female sex could not, therefore be established in our study although, among the more severely involved patients who had to be admitted to the hospital 19 were women as compared to 14 men. The



Fig. 3—Common site of lesion due to trauma



Fig. 4—Ulcer complicated by erysipelas, with necrosis of tendons

majority of the patients were young healthy strong normally built and in a satisfactory state of nutrition.

At the time of the patients' admission, the ulcers had been present for periods of from five weeks to one and a half years.

In 1 case colitis had preceded the development of the ulcer, and it recurred during the period of treatment. No amebas or tubercle

bacilli were found in the feces. In another case there was associated pellagra and in 2 others Burgei's disease. In the latter no doubt, the underlying disturbance had to be held responsible for the production of the ulcer but apparently streptococcic invasion had supervened so

TABLE 2—*Age Distribution in Fifty-Eight Cases of Phagedenic Ulcer*

Age of Patient	No of Cases
0 to 10 years	3
10 to 20 years	19
20 to 30 years	13
30 to 40 years	11
40 to 50 years	7
50 to 60 years	3
Total	58



Fig. 5—*Ulcus phagedenicum cutis*

that further development was perfectly parallel to that observed in our other patients.

In 25 cases traumatism could be traced as the exciting cause while in the others the patients were unable to give any information as to causation. The primary injury was, as a rule, reported in the malleolar region or over the tibia and was caused by stones, non bicycle accidents, barbed wire, mosquito bites or, as in 1 case, a dog bite. Other causes were injection of milk phlegmon or operation on deformed feet.

From the description of patients from whom intelligent information could be extracted the following characteristic picture emerged. The first injury was as a rule, an ordinary contusion occasionally accompanied with insignificant hematomas without erosion of the skin. It was only after renewed trauma had involved the same place some-



Fig 6—Ulcus phagedenicum cutis



Fig 7—Acanthotic epithelium overlapping edges of ulcer. An acute inflammatory process in the cutis

times weeks later with injury to the skin that the ulcers had developed and could not be brought to heal. Some of the patients, however, reported that the ulcers developed after the first injury.

Colitis was only once recorded as a forerunner in our cases, a situation not in accordance with the data published in the literature.

*Bacteriology* Extensive bacteriologic examinations were possible in 44 cases. Cultures were made on blood plates as well as on anaerobic culture mediums, on bouillon and agar. The procedure was to take material from the center of the ulcer and from underneath the undermined edges separately and to inoculate the portions separately into the culture mediums. It was seen that findings in the periphery substantially differed from those of the center. In fresh, not yet treated, cases hemolytic streptococci were the sole organisms, later disappearing from the center, where their place was occupied by *Staphylococcus aureus*, while in the recesses beneath the overhanging edges they continued to be present. In areas where corridors had developed, the skin over them was punctured and material aspirated from the depth with a syringe, hence, we were often able to obtain pure cultures of the bacterial flora of these corridors. In the 44 cases which were examined bacterial findings were the following:

	No. Cases
Hemolytic streptococci and <i>Staphylococcus aureus</i>	17
Hemolytic streptococci alone	3
<i>Staph. aureus</i> alone	7
<i>Str. anaerobius</i> and <i>Staph. aureus</i>	4
<i>B. proteus</i> and <i>Staph. aureus</i>	4
<i>B. proteus</i> alone	4
<i>B. coli</i> and <i>Staph. aureus</i>	1
<i>Staph. albus</i> and <i>B. pyocyaneus</i>	1
<i>Staph. albus</i> alone	1
<i>Pneumococcus</i>	1
Sterile	1
Total	44

In more than half the cases, therefore, hemolytic streptococci or *Str. anaerobius* was found in symbiosis with *Staph. aureus* or either of them separately. In this respect our results show a high degree of concordance with those collected by Touraine and co-workers<sup>1</sup> from the literature.

A definite parallelism could be established between bacterial findings and the course of the disease. As long as hemolytic streptococci were present, new spreading to the periphery was recorded again and again. In a number of cases the process would apparently come to a standstill peripherally, to be all of a sudden interrupted by new outbursts. As a response to therapeutic measures hemolytic streptococci were first to

1 Touraine, A., and Duperrat, R. La gangrene post-opératoire progressive de la peau. *Ann. de dermat. et syph.* **10** 257-285 (April) 1939. Touraine, A. Lortat-Jacob, E., and Neret. La gangrene microbienne insulaire bénigne de la peau, *Bull. Soc. franç. de dermat. et syph.* **45** 1022-1026 (June) 1938.

disappear, while *Staph aureus* followed more slowly. Then occasionally *B. proteus* would make a transitory appearance for shorter or longer periods until the ulcer was eventually sterile. The observations tabulated are, for the greatest part those of the initial stages, e.g., prior to treatment. If secondary contamination was suspected we applied compresses soaked in isotonic solution of three chlorides which were left on the ulcer for a few days, and now and then it was possible, after two to three days of this treatment to obtain pure cultures of hemolytic streptococci or *Staph aureus*.

*Histologic Examination*—In 14 cases biopsy specimens were taken from the edges as well as from the floor of the ulcers. In the following paragraph is given the histologic report (Pathological Institute, Head Professor Franco)

The histologic picture is that of chronic, subacute inflammation with ulceration but without evidence of specificity. The inflammatory process extends over the whole width of the specimen. Between the infiltrating cells there are fine epithelial bands isolated from each other by inflammatory tissue giving the impression of a retrograde development.

In figure 1 one sees the epithelium overlapping the edges of the ulcer with a tendency to grow into the depth. Microscopic conditions explain the aspect, as it presents itself to the naked eye, of an ulcer with undermined edges. The whole width of the cutis shows decided infiltration, indicating a subacute inflammatory process (plasma cells, histiocytes, leukocytes and a few granulocytes). The granulocytes are in particularly great number present at the edges of the ulcer together with red blood corpuscles, their number and distribution varying from one place to the other.

Figure 8 shows an area of subcutaneous adipose tissue, with particularly decided inflammation. Note the extensive cell infiltration.

*Differential diagnosis*—During the desert war in the Near East a number of ulcerations reported were generally included in the group of "desert sores." In reality, they represent ulcers of widely varying causation but in the main belonging to the three well known groups: tropical ulcers, diphtheritic ulcers and those called by us - "phagedenic ulcers." The distinction of the last from tropical ulcers seems to be the most important issue from the differential diagnostic standpoint. *Ulcus tropicum fusospirillosum* also develops in the malleolar or tibial region, likewise appearing singly. Its floor is, however, covered with a dirty gray gelatinous membrane, it is of oval shape and sharply outlined with no undermining of the edges. It causes, moreover, extraordinarily violent pain so that often narcotics have to

2 Dostrovsky, A., and Sagher, F. Phagedenic Ulcer (Pvoderma Gangraenosum). Treatment with Sulfapyridine Powder and Moist Chamber Therapy. Arch. Dermat. & Syph. 48 164-172 (Aug) 1943.

be taken Kerby<sup>3</sup> identified spirochetes as well as fusiform bacilli micrococci and other bacteria in them, and so did Brown<sup>4</sup> in half the number of his cases. In this country the disease has been studied by Garry,<sup>5</sup> Berlin<sup>6</sup> and Blum,<sup>7</sup> whose publications on the subject contain much valuable information.

Although bacteriologic specimens were again and again studied by us, we were in no case able to detect spirochetes or fusiform bacilli. In the great number of references to the lesion found in the literature,

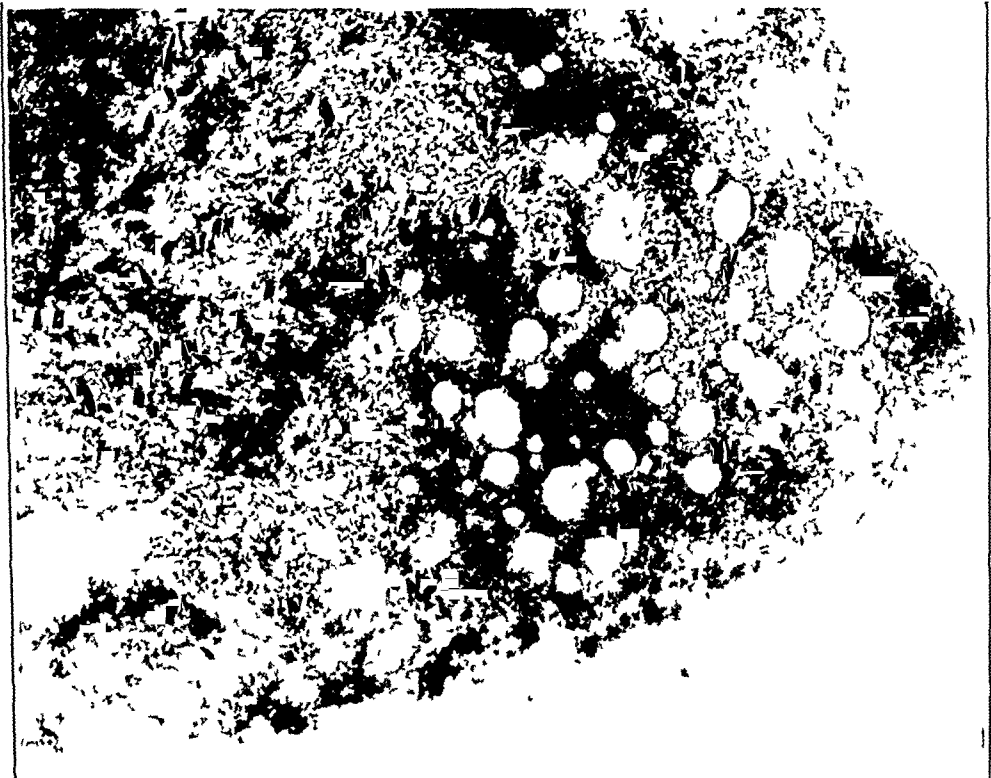


Fig 8—Decided inflammation in adipose tissue

particularly from tropical regions, now and then the two types seem to have been confused and included in one and the same group under the heading "tropical ulcer." That the two types are, however,

3 Kerby, T. R. F. *Ulcus Tropicum*, *Lancet* **1** 235-237 (Jan 30) 1932.

4 Brown, A. A. F. *Ulcer Syndrome in Tropical Africa*, *J. Trop. Med.* **38** 157 (July 1) 1935, 170 (July 15) 1935, 187 (Aug 1) 1935, 201 (Aug 15) 1935, 215 (Sept 2) 1935.

5 Garry, G. *Ulcus Epidemicum*, *Arch. f. Schiffs- u. Tropen-Hyg.* **34** 351-354 (July) 1930.

6 Berlin, C. *Ulcus Tropicum and Its Treatment*. Report of Epidemic 1934, *Harefuah* **11** 11-111 (Nov) 1936.

7 Blum, I. (a) A Seldom Form of Chronic Ulcer of Skin Due to *Streptococcus Micro-Aerophilus*, *Harefuah* **23** 153-154 (Nov 15) 1942, (b) The Differential Diagnosis of Some Infectious Ulcers of the Skin, *ibid.* **25** 90-91 (Sept 1) 1943.

definitely different as to their pathogenesis is shown by experiments conducted by Smith,<sup>8</sup> who was able to produce tropical ulcers by inoculation of cultures of fusiform bacilli and spirochetes

Diphtheritic ulcers, which in the subtropical zones are not rare, may be recognized by the slight or altogether absent undermining of the edges, which are, as a rule, thickened, further by their constant shape and the grayish membrane with which they are covered, often firmly attached to the floor, as well as by the slight degree of discharge from the surface

A similar aspect is presented by the so-called "pyoderma chancriformis faciei" (Hoffmann<sup>9</sup>), although this lesion is more superficial, indurated and accompanied with distinct swelling of the lymph nodes. Moreover, localization in the face has never been encountered in our cases, while in the type referred to by Hoffmann<sup>9</sup> it is characteristically restricted to that region

What has been described as "pyoderma gangrenosum" (Brunsting, Goeckerman and O'Leary<sup>10</sup>) presents conditions, clinically as well as bacteriologically, similar to those found in our cases. Whether the lesions described by Meleney<sup>11</sup> can be distinguished from those of our group on the grounds of the slight deviations in their clinical picture is doubtful. Probably the two lesions represent variations of one and the same process which have been named differently. Postoperative progressive gangrene has, therefore, also been included by us in this group. In the same way as is the case with spontaneous ulcers it is caused by trauma, here provided by operation

Meleney<sup>11</sup> and Cullen<sup>12</sup> reported lesions of this type on the abdomen, particularly occurring after drainage of abscesses or empyema.

8 Smith, E. C. Inoculation Experiments with *Bacillus Fusiformis* Isolated from Tropical Ulcer with Observations on *Bacillus*, *J Hyg* **33** 95-102 (Jan) 1933

9 Hoffmann, E. Isolierte schankeraehnliche Pyodermie der Gesichtshaut (Pyoderma chancriformis faciei), *Arch f Dermat u Syph* **170** 403-409, 1934

10 Brunsting, L. A. Goeckerman, W. H. and O'Leary, P. A. Pyoderma (Ecthyma) Gangrenosum. Clinical and Experimental Observations in Five Cases Occurring in Adults, *Arch Dermat & Syph* **22** 655-680 (Oct) 1930

11 (a) Meleney, F. L. Hemolytic *Streptococcus* Gangrene, *Arch Surg* **9** 317-364 (Sept) 1924, (b) Differential Diagnosis Between Certain Types of Infectious Gangrene of Skin, with Particular Reference to Haemolytic *Streptococcus* Gangrene and Bacterial Synergistic Gangrene, *Surg, Gynec & Obst* **56** 847-867 (May) 1933. (c) Meleney, F. L., and Johnson, B. A. Further Laboratory and Clinical Experiences in Treatment of Chronic Undermining, Burrowing Ulcers with Zinc Peroxide, *Surgery* **1** 169-221 (Feb) 1937

12 Cullen, T. S. Progressively Enlarging Ulcer of Abdominal Wall Involving Skin and Fat, Following Drainage of Abdominal Abscess Apparently of Appendiceal Origin, *Surg, Gynec & Obst* **38** 579-582 (May) 1924

as well as after drainage of the abscess. Schmidt's<sup>13</sup> case presented colitis and carcinoma, and it was in the operative wound that the gangrenous ulcer appeared. A similar development is found in 1 of our cases.

In our case, after operation for mammary carcinoma with subsequent drainage, an ulcer developed, which in the course of two and a half months laid bare the whole of the chest wall on the right side and, apart from a disastrously progressive tendency and extensive undermining of the edges, spread also to the depth leading to pyopneumothorax with erosion of small blood vessels to which the patient eventually succumbed (fig. 9).



Fig. 9—Ulcer developing two and a half months after operation for carcinoma.

*Therapy.* After initial attempts to influence the ulcers by zinc peroxide treatment, the onset of the sulfanilamide era induced us to start oral and intramuscular as well as local sulfanilamide therapy too and we saw rapid disappearance of the bacterial flora from the ulcers treated by this method. When sulfanilamide, sulfapyridine or sulfathiazole powders are employed, it is imperative that an intimate contact be established between the powder and the parts to be treated. The powder should be introduced in a way that actually insures its reaching all the nooks and corners beneath the undermined edges of the ulcer by a sound or spatula, deep underneath the overhanging edges, and

13 Schmidt, H. W. Hyperimmune Streptococcic Serum in Treatment of Pyoderma Gangrenosa Associated with Chronic Ulcerative Colitis and Carcinoma of Colon, Proc. Staff Meet., Mayo Clin. **11** 244-247 (April 15) 1936.



applications should be repeated every twenty-four hours, until the ulcer has been rendered sterile, which, as a rule requires three weeks. To stimulate granulation we employed the moist chamber method. Although this was no "quick method" it was possible to get the disease under control and to forestall further outbreaks so that in the end retrogression could be enforced. It became moreover clear that removal of the undermined edges by means of surgical manipulations was unnecessary since the detached parts often grew together again.

## COMMENT

Reference to the disease is found in the literature under many different designations, from Brocq<sup>14</sup> up to very recent times but neither the clinic the pathogenic nor the bacteriologic study yields a uniform picture. It is not only under different designations but under one and the same, too that wide variations have been described. It is our endeavor by including characteristic photographs showing the lesion at various sites and giving a good illustration of its special properties, to outline a typical picture of the disease thus facilitating its distinction from other diseases.

There is no consensus as to what persons are generally attacked by the disease. Touraine and co-workers<sup>1</sup> stressed its preponderant occurrence in women over 50 years of age, while Cohen<sup>15</sup> drew attention to its prevalence in young girls. Meleney<sup>11</sup> on the other hand pointed out that the lesion may be encountered at any age in an equal measure in both sexes and anywhere on the body surface. Our material does not give any indication as to the prevalence in one sex or a special age group either but gives evidence of predilection for the malleolar and tibial regions, although any other part of the body may equally be attacked.

As to the existing cause opinions are also at variance. Sachs<sup>16</sup> saw an ulcer of this kind develop in a girl who showed no constitutional stigmas and, after the lapse of four years heal in an equally inexplicable manner. Meleney,<sup>11</sup> Sutton<sup>17</sup> and Touraine and co-workers<sup>1</sup> report occurrence subsequent to traumatism with no previous circulatory disturbance being reported in the areas involved. The trauma may

14 Brocq, L. Nouvelle contribution a l'etude du phagedenisme geometrique, *Ann de dermat et syph* **6** 1-39 1916-1917, cited by Greenbaum<sup>26</sup>

15 Cohen, M. H. Pyoderma Gangraenosum. A Deficiency Disease Complex. *Arch Dermat & Syph* **33** 813-824 (May) 1936

16 Sachs, W. Sphaceloderma. Report of Case of Unusual Phagedenic Ulceration of Skin, Subcutaneous Tissue and Muscle of Chest Wall, *Arch Dermat & Syph* **33** 977-987 (June) 1936

17 Sutton, R., and Sutton, R., Jr. Diseases of the Skin, ed 9, St. Louis C. V. Mosby Company, 1935

be a mechanical one, it may also be provided by burns or operations. The majority of authors concerned with the subject describe their occurrence simultaneously with or as a consequence of chronic colitis. Jankelson and McClure<sup>18</sup> gave details of 7 cases of chronic idiopathic ulcerative colitis in which cutaneous ulcers developed when the infection was at its peak, in 4 cases disappearing during remissions of the underlying disease.

In the cases of Brunsting, Goeckerman and O'Leary<sup>19</sup> associated colitis was reported four times and empyema once. Weiner's<sup>19</sup> patient was also suffering from colitis, and Barger<sup>20</sup> found, among 150 cases of colitis, 12 which presented phagedenic ulcers. McCarthy<sup>21</sup> pointed out that the state of reduced resistance, created by colitis of prolonged duration, favors the development of large ulcers of the skin. It is possible that in patients suffering from colitis inadequate absorption may lead to vitamin deficiency, which does not, however, imply that the ulcers should be considered a direct consequence of this deficiency. Cohen<sup>17</sup> maintained that colitis, ulcers and hypochromic anemia form a pathologic triad. In his case there was atrophy of the tongue, the disease could not, however, be influenced by vitamin administrations as he assumed, owing to the disturbed intestinal absorption. The majority of our patients were otherwise healthy, with no constitutional stigmas presenting evidence of internal disease.

There is a greater agreement of opinion in regard to bacterial findings. Although the number of germs held responsible for the production of the lesion is large, attention is in an increasing measure being focused on the fact that certain bacterial groups, either separately or in combination, are of vital importance. Brunsting and co-workers,<sup>19</sup> Brewer and Meleney<sup>22</sup> and Fox<sup>23</sup> attached particular significance to the symbiosis of hemolytic streptococci and *Staph aureus*. Touraine and co-workers<sup>1</sup> gave a tabulation of 81 cases from the literature, 38 of which showed streptococci and staphylococci in symbiosis while in 16 streptococcus occurred in combination with other nonstaphylococcic infections, and eventually, in 8 cases, staphylococci were found in pure culture or in combination with other nonstreptococcic germs.

18 Jankelson, I. R., and McClure, C. W. Skin Lesions During Course of Ulcerative Colitis, *Acta dermat-venereol* **21** 255-267 (March) 1940.

19 Weiner, A. L. Pyoderma Gangraenosum Treated with Sulfanilamide. Report of Case, *Arch Dermat & Syph* **41** 711-717 (April) 1940.

20 Barger, J. A., in discussion on Schmidt<sup>13</sup>.

21 McCarthy, L., and Fields, R. Pyoderma Gangrenosum, *New York State J Med* **31** 801-804 (July 1) 1931.

22 Brewer, G. E., and Meleney, F. L. Progressive Gangrenous Infection of Skin and Subcutaneous Tissues, Following Operation for Acute Perforative Appendicitis. Study in Symbiosis, *Ann Surg* **84** 438-450 (Sept.) 1926.

23 Fox, H., in discussion on Cipollaro<sup>28</sup>.

Lane and Stroud<sup>24</sup> found hemolytic *Staph albus* and streptococci while Gibson<sup>25</sup> found *Staph albus* only. Greenbaum,<sup>26</sup> who devoted a great amount of attention to this question came to the conclusion that possibly streptococci and staphylococci act in conjunction but only if certain particular conditions are fulfilled, allowing the germs to display their activity and to produce the disease. Greenbaum<sup>26</sup> reported on 6 cases with similar bacterial findings. By inoculation it was possible to produce similar ulcers in the same patient at distant sites with streptococci and staphylococci in association but not however, with one of the strains alone. In 1 case hemolytic *Str aureus* and *B proteus*, inoculated separately provoked no reaction. In combination, however, they produced an ulcer from the surface of which the two germs could even be recultured. In 1 of our cases for experimental reasons material taken from underneath the undermined edges of the ulcer where hemolytic streptococci had been identified was applied to a scratch on the skin at a considerable distance from the original ulcer. The same procedure was adopted with material from the center (*Staph aureus*) and eventually a mixture of the two materials was applied to a third scratch. All the experiments, although each one was repeated twice yielded negative results, i. e., there was no local reaction at all to the inoculations.

Brewer and Meleney<sup>27</sup> stated the belief that the significance of the bacterial flora lies in the fact that hemolytic streptococci prepares the ground for the activity of *Staph aureus*, which then continues the work of destruction. Bloom<sup>28</sup> does not support the etiologic role of the bacterial flora but stresses the importance of the presence of other diseases such as syphilis, tuberculosis, colitis and in the case demonstrated by Cipollaro<sup>28</sup> meningitis and mastoiditis.

A certain amount of significance might be attached to experiments on animals set up to clarify the question. Brunsting and co-workers,<sup>10</sup> using a combination of the two germs, were able to produce ulcers in their experimental animals similar to those found in human beings. Brewer and Meleney<sup>27</sup> found it possible to produce in guinea pigs and in rabbits and in one instance, in a dog ulcers by combined inoculations.

24 Lane C W and Stroud, C M. *Pyoderma Gangrenosum*. Report of Case. *Arch Dermat & Syph* **27** 460-471 (March) 1933.

25 Gibson R. *Pyoderma Gangrenosa*, *Brit J Dermat* **49** 560-563 (Dec) 1937.

26 Greenbaum S S. *Phagedaena Geometrica* (Brocq). Inoculation Studies with Viable Bacteria Cultured from Lesions of *Phagedaena Geometrica* (Brocq) (Chronic Burrowing Ulcer and *Pyoderma Gangraenosum*), *Arch Dermat & Syph* **43** 775-801 (May) 1941.

27 Bloom D. in discussion on Cipollaro<sup>28</sup>.

28 Cipollaro A C. *Pyoderma Gangraenosum*, *Arch Dermat & Syph* **43** 860-862 (May) 1941.

of nonhemolytic microaerophilic streptococci and hemolytic *St. aureus*. Any of these strains applied separately rarely produced gangrene in the case of *Staph. aureus*, while with streptococcus this was altogether impossible.

Lane<sup>29</sup> successfully employed *St. hemolyticus* vaccine (intracutaneously) in a concentration of 1:1,000 to provoke specific cutaneous reactions.

Whether special etiologic significance should be attached to the bacterial flora is, therefore, not altogether clear in view of the aforementioned data. The results of our own bacteriologic examinations were varied enough, although there was a definite preponderance of streptococci and staphylococci either alone or in symbiosis with each other. Our tabulation gives no indication of the frequency with which *B. proteus* has been encountered. Though in the initial stage it is not frequently met with in the majority of cases it makes its appearance in the course of time. It may well be that it is initially suppressed by staphylococci and streptococci. Another striking feature is, moreover, the stubborn resistance of *B. proteus* against any attempt of therapy once it has established itself on the ulcer. The therapeutic measures instituted to influence the streptococcic flora had only one clear result in that it was only after their departure that the ulcer could be induced to heal.

The question as to why healing of these ulcers constitutes such a difficult problem is therefore, still unanswered. A possible explanation may be that the activity of streptococci consists in a certain influence on the blood vessels, thus interfering with the supply of blood to the areas involved. On the other hand, the first injury may be the cause of the primary cellular lesion so that later supervening bacterial invasion may display its full weight. The matter is certainly rather intricate which is characteristically illustrated by the following case history.

The patient was a boy of 14 who had always been healthy. Two years earlier he had, however, had osteomyelitis of the hip joint region which was cured but with reduced mobility of the joint. Three months before we saw him he fell and hurt himself in the neighborhood of the left trochanter where swelling subsequently developed. This swelling was punctured by a surgeon, and some blood withdrawn. Later, however, puncture revealed pus. A few days later an ulcer developed at the place of the injury, spreading geometrically and eventually reaching a size of 5 to 6 cm. The edges appeared as though they were punched and were extensively undermined down to the fascia. There was no swelling of lymph nodes nor pain.

29 Lane, C. G. Spontaneous Necrotic Dermatitis (Hemolytic Streptococcus). *Arch. Dermat. & Syph.* **41**: 414-415 (Feb.) 1940.

The patient had been treated with sulfanilamide at the surgical department. When he was admitted to the dermatologic department, bacteriologic examination revealed *Staph aureus*.

As is seen from the history there had originally been an injury, but the surgeon in charge of the case reported that the skin had been unchanged up to the time of the first puncture. In this patient we might consider the possibility that we are dealing with a tissue reaction on the lines of the Shwartzman<sup>30</sup> phenomenon arising on the grounds of the previous osteomyelitis.

#### SUMMARY

1 Details are given of 58 cases of a chronic ulcerative disease, consisting in the main of progressive, destructive lesions of the skin, occasionally down to the fascia, with deeply undermined edges. The ulcers appear in various locations, preponderantly the lower extremities, and usually in otherwise healthy persons. The outstanding feature of these lesions is phagedenization, hence we propose the name "phagedenic ulcer."

2 Differential diagnostic distinction of the lesion from other ulcers occurring in subtropical regions is discussed. They should be distinguished from diphtheritic ulcers with their grayish membranes, absence of progressive spread and characteristic microscopic changes. On the other hand, a distinction should be made from tropical ulcers with their characteristically circular outline, foul-smelling slough, rapid development and typical micro-organisms.

3 Attention is drawn to the possibility of a similarity of this disease to pyoderma gangrenosum or Meleney's ulcer, in spite of the absence of gastrointestinal symptoms, the variety in the clinical aspect and the occasional absence of the typical bacterial flora described for the two last-mentioned diseases.

4 It is emphasized that the factors known to be relevant to the causation of the disease have only pathogenetic significance, and we maintain that there may still be another, as yet unclarified, etiologic factor.

Professor Franco, Head of the Institute of Pathological Anatomy, and Dr Gurevitch, Head of the Bacteriological Department, both of the Rothschild-Hadassah University Hospital, assisted in the bacteriologic and histologic examinations.

30 Shwartzman, G. The Phenomenon of Local Skin Reactivity to *Streptococcus Hemolyticus-Scarlatinae*, *J Infect Dis* **48** 183-188 (Feb) 1931.

## VITAMIN B COMPLEX IN THE TREATMENT OF LICHENOID DERMATITIS

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A LARGE number of cases of dermatologic diseases developed among the American troops stationed on the Southwest Pacific island of New Guinea and the small islands adjacent for a radius of several hundred miles in the years 1943, 1944 and 1945. In this group of skin diseases a lichenoid form of dermatitis stood out as a major medical problem. It usually appeared in persons who had been in New Guinea for at least three months and in most cases on an average of nine to twelve months or longer. The soldiers affected had been taking quinacrine hydrochloride (atabrine) regularly for the suppression of malaria and were living solely on K or C rations for months at a time under field conditions in the tropical jungle, and fresh meat, vegetables and fruits were practically never included in their diets. Almost all the patients had lost from 10 to 40 pounds (4.5 to 18 Kg) of weight after reaching the tropics. The same disease was seen in other war theaters where soldiers were taking quinacrine hydrochloride.

The eruption usually began on the hands or feet or simultaneously on both hands and feet as a simple patch of erythema alone or as erythematous patches with vesicles and pruritus. In most cases the lesions would at first be mild and remain localized for weeks or months, and then some extension would take place to other adjacent areas, or when the disease was severe to the entire body. The lesions on the hands and feet were chiefly localized to the dorsal surfaces, and the distribution was suggestive of pellagra. The eruption often went through an exudative moist phase in the first few months, followed by a drying of all the moist areas and the production of three distinct types of morphologic entities thereafter. The commonest type was a severe dry scaling patchy erythematous dermatitis scattered over the dorsal surfaces of the hands, feet, legs, forearms and other areas of the body. This resembled a subacute eczema in its appearance and has been com-

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monly called eczematoid dermatitis. A second common type was a violaceous nodular and papular lichen planus form of eruption with pronounced pigmentary changes of the skin and lesions of the mucous membrane typical of lichen planus. This type clinically resembled severe hypertrophic lichen planus and was often generalized in distribution. The third or mixed, type was a combination of the lesions of the eczematoid and lichen planus types in the same patient. All three types itched severely, often had a moist oozing phase and became secondarily infected and frequently went on to a generalized severe exfoliative dermatitis. In most cases the eruptions were resistant to any type of treatment employed in the New Guinea area, and a large number of the patients were returned to the United States. Many patients had clearing or improvement of their eruptions while en route to the United States, or recovery following treatment in various army general hospitals in the United States after their return.

Because of the distribution and pellagra-like appearance of some of the lesions, the lack of fresh fruits, vegetables, eggs, milk and meat in the diet for long periods, the tendency of the soldiers to eat native foods instead of rations balanced in vitamin content, and the common tendency to eat inadequate amounts of rations, we suspected that avitaminosis might play a part in the cause of the dermatitis or be a contributing factor in prolonging the eruption. Consequently, it was decided to survey all patients admitted to the dermatologic ward at DeWitt General Hospital by means of a form which summarized each patient's entire history and course of hospitalization. This form included the date of onset of the cutaneous lesions, the dates of hospitalization in New Guinea, a description of the lesions at onset as to type, location, development and subsequent distribution and the type and duration of the field diet overseas, with a notation of the presence or absence of fresh foods, any history of malaria, dysentery, secondary infection of the dermatitis, fever, edema and loss of weight and the general physical condition overseas. Abnormal laboratory observations, the type of treatment overseas, the dose of quinine hydrochloride and the duration of quinine therapy were also noted. On admission to DeWitt General Hospital each patient was photographed and biopsies of the cutaneous lesions were taken. The course in the hospital, including the details of the treatment employed, was recorded daily. The 48 patients studied were divided into two groups, chosen alternately, both of which received routine standard dermatologic care, the details of the therapy depending on the type of case as previously noted and whether the stage of the disease present was acute, subacute or chronic. This local dermatologic care consisted of compresses, soaks, lotions, pastes and simple ointments, the exact treatment varying with the individual indications in each case. Roentgen ray therapy was employed in two thirds of the cases.

in which the chronic lichenified lesions responded slowly to local treatment. One of the two groups received, in addition to the local therapy, the following regimen of vitamin B complex therapy: (a) tablets, thiamine hydrochloride, 5 mg twice daily, (b) yeast tablets, 3 Gm daily, (c) riboflavin, 5 mg, with nicotinamide 200 mg (Lilly<sup>1</sup>) daily, intramuscularly, (d) extract of liver (Lederle concentrate, 10 units per cubic centimeter) 2 cc intramuscularly, three times weekly, and (e) raw liver, 100 Gm daily, specially prepared by the dietitian to promote palatability. At the time this treatment was instituted, all the patients had had their cutaneous lesions for from four to eighteen

TABLE 1—*Summary of Data on Patients with Lichenoid Dermatitis Receiving Routine Dermatologic Care (Group I)*

Patient Number	Type of Eruption	Duration of Disease, Months	Severity	Time in Hospital, Weeks
1	Lichen planus	15	Severe	12
2	Eczematoid	11	Severe	16
3	Eczematoid	7	Severe	16
4	Lichen planus	9	Moderate	10
5	Lichen planus	12	Moderate	11
6	Lichen planus	18	Moderate	6
7	Eczematoid	5	Moderate	10
8	Eczematoid	7	Moderate	8
9	Lichen planus	5	Moderate	5
10	Eczematoid	8	Moderate	5
11	Eczematoid	6	Moderate	5
12	Lichen planus	5	Moderate	9
13	Eczematoid	1	Moderate	7
14	Eczematoid	6	Moderate	4
15	Eczematoid	7	Moderate	13
16	Eczematoid	9	Moderate	5
17	Eczematoid	6	Mild	8
18	Eczematoid	8	Mild	4
19	Eczematoid	11	Mild	6
20	Eczematoid	15	Mild	7
21	Eczematoid	5	Mild	9
22	Eczematoid	8	Mild	4
23	Eczematoid	1	Mild	5
24	Eczematoid	4	Mild	8
25	Eczematoid	9	Mild	4
26	Eczematoid	6	Mild	5

months. None of them were taking quinacrine hydrochloride. For purposes of comparison, the eruptions of all of the 48 patients were graded into three groups, mild, moderate or severe, depending on extent and severity. The patients with mild eruptions were those with lesions on the hands or feet alone or on both hands and feet. Those graded as having moderate eruptions had lesions involving one third to one half of the body area, while those with severe eruptions had extensive generalized and severe involvement.

Of the 48 patients who were included in this study 22 (group II) of them received the vitamin B complex regimen in addition to their local dermatologic treatment, and 26 (group I) received only the local

1. Riboflavin with nicotinamide ampules were furnished through the courtesy of Eli Lilly and Company, Indianapolis.



dermatologic treatment. Group II consisted of 4 patients with severe eruptions, 11 with moderate eruptions and 7 with mild eruptions with an incidence of lichen planus lesions as follows: 1 with severe eruptions, 3 with moderate eruptions and 1 with mild eruptions. All the others had lesions of the eczematoid type except 1 with a severe eruption which was a generalized exfoliative dermatitis. In the control series of 26 patients (group I) there were 3 with severe eruptions, 13 with moderate eruptions and 10 with mild eruptions. One of the severe eruptions was of the lichen planus type and five of the moderate eruptions were also lichen planus in type. There were no patients with mild lichen planus lesions in this group. No patient with a mixed type of

TABLE 2—*Summary of Data on Patients with Lichenoid Dermatitis Receiving Routine Dermatologic Care and Supplemental Vitamin B Complex (Group II)*

Patient Number	Type of Eruption	Duration of Disease, Months	Severity	Time in Hospital, Weeks
1	Lichen planus	8	Severe	16
2	Eczematoid	6	Severe	14
3	Eczematoid	9	Severe	12
4	Exfoliative	5	Severe	16
5	Lichen planus	7	Moderate	8
6	Eczematoid	4	Moderate	4
7	Eczematoid	6	Moderate	4
8	Eczematoid	9	Moderate	6
9	Lichen planus	10	Moderate	5
10	Eczematoid	7	Moderate	6
11	Eczematoid	5	Moderate	7
12	Eczematoid	8	Moderate	8
13	Eczematoid	15	Moderate	5
14	Eczematoid	7	Moderate	4
15	Lichen planus	5	Moderate	9
16	Eczematoid	15	Mild	5
17	Eczematoid	6	Mild	5
18	Eczematoid	4	Mild	4
19	Lichen planus	9	Mild	4
20	Eczematoid	7	Mild	6
21	Eczematoid	9	Mild	2
22	Eczematoid	6	Mild	4

eruption was employed in this study. Direct examination of scrapings of the skin in a 10 per cent solution of potassium hydroxide and cultures were negative for pathogenic fungi in all cases. For all the patients in both groups roentgenologic studies of the small intestine were made with use of barium sulfate as a contrast medium in order to determine whether changes existed which might be related to a deficient absorption of food. In 8 of the 48 patients hypermotility was found, but in only 3 of these was it of sufficient degree to have possible pathologic significance. In view of the observations, the roentgenologic studies suggest that a deficient absorption of food did not play a major role in causing the disability.

All patients in both groups were observed to gain weight rapidly while receiving regular diets in the hospital. The cutaneous lesions began to disappear fairly rapidly in most instances, regardless of

whether or not vitamin B complex was administered. However, a statistical analysis of the recovery rate in the two groups of patients disclosed that those with mild eruptions, receiving routine dermatologic care alone, recovered completely in an average of six weeks while the group receiving vitamin B complex plus routine dermatologic care recovered in an average of four weeks. The patients with moderate eruptions recovered in an average of eight weeks with only routine dermatologic care and in six weeks with the administration of vitamin B complex. Those with severe eruptions took on an average of twelve to sixteen weeks to recover, and the administration of vitamin B complex seemed to make little difference in the time of recovery. All patients except 2 with severe eruptions included in this study recovered completely and were returned to duty, which in most instances was permanent limited duty in the United States. Of the 2 who did not improve satisfactorily, 1 with a severe eczematoid type of eruption did recover after twelve months of continuous treatment. The other, with a severe lichen planus type of eruption, also recovered after twelve months of treatment.

## COMMENT

There are a number of reports in the literature dealing with the relationship between vitamin B deficiency and dermatitis. Birch, Gyorgy and Harris,<sup>2</sup> as well as Dann,<sup>3</sup> demonstrated that pyridoxine deficiency leads to the development of dermatitis in rats. Elvehjem, Madden, Strong and Woolley<sup>4</sup> showed that nicotinic acid is the anti-black-tongue and pellagra-preventive factor. Riboflavin is indispensable for human beings and animals alike, and its lack, according to Sebiell and Butler,<sup>5</sup> produces a typical dermatosis in human beings. So-called tropical avitaminosis, as stated by Wright,<sup>6</sup> is a polyavitaminosis manifested by a glazed, sore tongue, sore angles of the mouth, eczema of the anus, scrotum and vulva, rough keratotic skin of the extensor surfaces of the forearms and thighs, a glazed varnished condition of the canthi

2 Birch, T. W., Gyorgy, P., and Harris, L. J. The Vitamin B<sub>2</sub> Complex. Differentiation of the Antiblacktongue and the "P-P" Factors from Lactoflavin and Vitamin B<sub>6</sub> (So-Called "Rat Pellagra" Factor), *Biochem J* **29** 2830 (Dec.) 1935

3 Dann, W. J. The Vitamin G Complex. The Nonidentity of Rat Dermatitis Due to Vitamin B<sub>6</sub> Deficiency and the Dermatitis of Human Pellagra, *J Nutrition* **11** 451 (May) 1936

4 Elvehjem, C. A., Madden, R. J., Strong, F. M., and Woolley, D. W. Relation of Nicotinic Acid and Nicotinic Acid Amide to Canine Black Tongue, *J Am Chem Soc* **39** 1767 (Sept.) 1939

5 Sebiell, W. H., Jr., and Butler, R. E. Riboflavin Deficiency in Man (Ariboflavinosis), *Pub Health Rep* **54** 2121 (Dec. 1) 1939

6 Wright, E. J. Polyavitaminosis and Asulphurosis, *Brit M J* **2** 707 (Oct. 10) 1936

and conjunctivitis. Gross<sup>7</sup> summarized the changes of the skin due to deficiency of vitamin B complex as being pellagra, ariboflavinosis, tropical avitaminosis and the Plummer-Vinson syndrome. He mentioned the fact that a number of different nonpellagrous cutaneous lesions respond to therapy with extract of liver, indicating that vitamin B deficiency may be a factor in their production. In group I of his series were the extensive scaling erythematous patches of dermatitis of unknown cause, which are associated with follicular keratosis and which resemble pityriasis rubra pilaris. In his group II, some patients with seborrheic dermatitis responded to liver by parenteral injection. In his group III were cases of vitamin B complex deficiency with moniliasis of the skin. In his group IV he included seborrheic dermatitis of the vulvoanal areas and kraurosis vulvae, which he stated may be due to a combined deficiency of vitamins A and B. His last group included the seborrheic exacerbation seen after arsphenamine therapy for patients with syphilis and disappearing with liver therapy.

The actual cause of lichenoid dermatitis is unknown. Quinacrine hydrochloride, used for malaria-suppressive therapy, has been considered as a causative factor.<sup>8</sup> Other contributing factors are also under consideration. Among them are (1) nutritional deficiency, (2) the moist warm tropical climate, (3) contact dermatitis, (4) unidentified bacteria, a virus or fungus, and (5) photosensitivity. The present study shows that vitamin B complex deficiency probably plays some role in the production of lichenoid dermatitis or that the presence of vitamin B complex deficiency may delay healing of the skin after the original dermatitis has developed. In view of the lack of fresh foods in the diet of the patients in New Guinea for many months, the decided loss of weight, the atypical character and distribution of the lesions, plus the accelerated recovery time of patients with moderate and mild eruptions when vitamin B complex is administered, it is our opinion that some degree of vitamin B complex deficiency is probably present. In most cases when the deficient vitamin is supplied to a person suffering from lichenoid dermatitis, the lesions improve more rapidly than when that person eats an adequate diet with fresh foods included but without supplemental vitamin B complex in large amounts. Whether vitamin B complex deficiency is a primary or a secondary factor in the production of New Guinea lichenoid dermatitis remains unsettled as yet, although it appears most probable that it is a secondary factor which tends to hinder recovery of the cutaneous lesions. Which portion of the

7 Gross, P. Nonpellagrous Eruptions Due to Deficiency of Vitamin B Complex, *Arch Dermat & Syph* **43** 540 (March) 1941

8 Reactions Attributed to Atabrine, United States Army Subject Letter (SPMCB 441), Office of Surgeon General, July 19, 1945

vitamin B complex is the essential agent remains to be determined by future investigation

#### SUMMARY

Lichenoid dermatitis appeared among troops in the field who were subsisting on K or C rations without fresh foods for long periods and who had lost considerable weight. These troops had been taking quina-craine hydrochloride (atabrine) daily for months for the suppression of malaria. The disease begins on the dorsal surfaces of the extremities with erythema and vesicles, which may spread to involve other areas or even the entire body, in either an eczematoïd or lichen planus type of eruption or a combination of both types of lesions. A severe exfoliative dermatitis may and often does supervene in any type of case. Two groups of patients were employed in our study. One group of 26 patients received routine dermatologic care alone and served as a control group. The other group, of 22 patients, received supplemental vitamin B complex both orally and parenterally in addition to routine dermatologic care. Vitamin B complex in large amounts caused a more rapid recovery when used in conjunction with routine dermatologic care for mild and moderate eruptions than the use of routine dermatologic care alone. Patients with severe eruptions recovered, but the time of recovery was not shortened by the vitamin B complex therapy. The cause of the lichenoid dermatitis is believed to be quina-craine hydrochloride, however, vitamin B complex deficiency probably plays a secondary role in the production of the disease or in its failure to heal rapidly once it appears.

#### CONCLUSIONS

1 The time of recovery from lichenoid dermatitis is shortened by the administration of vitamin B complex in large doses in addition to routine dermatologic care. This improvement occurs in patients with moderate and mild eruptions but not in those with severe ones.

2 Vitamin B complex deficiency is a factor, probably secondary, in causing lichenoid dermatitis.

3 The fraction or fractions of the vitamin B complex group which are responsible for the more rapid recovery are yet to be determined.

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## PROGRESSIVE RECURRENT DERMATOFIBROMA (DARIER-FERRAND)

### Anatomoclinical Study

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AS OFTEN happens in dermatology, to the confusion of those who are beginning the study of this specialty, the cutaneous disease which I shall discuss in this paper is known by a large number of names. In Germany, for instance, it has been called fibrosarcoma (Vichow), fusocellular fibrosarcoma (Unna), fibroblastic sarcoma or sarcomatous fibroma (Zurhelle) and tuberous or protuberant fibrosarcoma or dermatofibrosarcoma (Hoffmann). In France it is described as progressive and recidivous dermatofibroma of Darier and Ferrand and fibrosarcoma of the skin<sup>1</sup>. Hertzler<sup>2</sup> has also described this disease under the name of sarcoma of the skin. These tumors have been described by Bezecky<sup>3</sup> as dermatofibrosis protuberans et progrediens. McMaster<sup>4</sup> has named them sarcomatoid fibroma of the skin, and Mosto<sup>5</sup> has called them neuroma or dermatoschwannoma.

### DEFINITION

According to Woringer,<sup>6</sup> progressive and recurring dermatofibromas are fibrous tumors of neoplastic evolution which develop on a fibrous plaque that in most cases begins several years earlier and is localized at the level of the abdominal wall. Its evolution is

1 Favre, M, and Josserand, A. Les fibrosarcomes de la peau, in Darier J, and others. *Nouvelle pratique dermatologique*, Paris, Masson & Cie, 1936, pt 6, pp 824-836.

2 Hertzler, A. E. Fibrosarcomatous Tumours of the Skin of the Trunk, Characterised by Attenuated Dermal Surfaces, *Ann Surg* **84** 489-496, 1926.

3 Bezecky, R. Dermatofibromatosis Protuberans et Progrediens, *Arch f Dermat u Syph* **162** 782-791, 1930.

4 McMaster, P. E. Sarcomatoid Fibroma of the Skin (Progressive and Recurring Dermatofibroma), *Ann Surg* **99** 338-347, 1934.

5 Mosto, D. Dermatoneurome, *Ann de dermat et syph* **10** 845-851, 1929, Sobre una nueva interpretacion de los dermatofibromas de Darier, *Semana med* **1** 855-859, 1929.

6 Woringer, F. Dermatofibromes progressifs et recidivants, in Darier, J, and others. *Nouvelle pratique dermatologique*, Paris, Masson & Cie, 1936, pt 6, pp 573-580.

progressive and extensive, and it is refractory to treatment. In spite of this, such tumors show only local malignant changes and do not give rise to metastases. It should be noted that progressive and recurring dermatofibromas, according to the observations of some authors, may give rise to cutaneous or internal metastases and that the initial phase is not always characterized by the classic fibrous plaque. Fidanza<sup>7</sup> has defined these tumors as lesions which, from the clinical point of view, are characterized by neoplasm of the skin whose objective aspect is peculiar and whose evolution is progressive and indefinite, according to him such tumors are refractory to treatment and show a strong tendency to recurrence after removal, denoting a certain amount of local malignant characteristics, they occur preferentially in the abdominal wall and inguinal regions.

#### HISTORICAL OUTLINE

The history can be divided into two stages. The first stage ends in 1924 with the appearance of the masterly paper of Darier and Ferrand<sup>8</sup>, the second is the stage which continues up to the present. The first phase is somewhat confused, for the problem had not yet been studied as a whole and in detail. According to Binkley,<sup>9</sup> Sherwell<sup>10</sup> in 1890 presented to the New York Dermatological Society a case for diagnosis and suggested that it was one of hypertrophic leprosy, a photograph of the patient was published in Piffard's book, but the case presents all the aspects of progressive and recurring dermatofibroma. In 1901 Johnston,<sup>11</sup> in a paper read before the Academy of Medicine of Buffalo and the American Dermatological Association, referred to a case in which he diagnosed the disease as myxosarcoma on account of the myxomatous degeneration which it showed. Later in 1903, Johnston<sup>12</sup> diagnosed the disease in his case as fibrosarcoma cutis and reported another typical case. In 1890 Taylor<sup>13</sup> reported a case. In 1904 Kartscher and Pfeiffer<sup>14</sup> reported cases in which they

7 Fidanza, E. P., Carrillo, F., and Ocana, T. Dermatofibromas progressivos e recidivantes de Darier, *Rev argent dermatosif* **19** 26-45, 1935.

8 Darier, J., and Ferrand, M. Dermatofibromes progressifs et récidivants ou fibrosarcomes de la peau, *Ann de dermat et syph* **5** 545-570, 1924.

9 Binkley, G. W. Dermatofibrosarcoma Protuberans, *Arch Dermat & Syph* **40** 578-594 (Oct.) 1939.

10 Sherwell, S. Morphea, *J Cutan & Genito-Urin Dis* **8** 72, 1890.

11 Johnston, J. C. Sarcoma and the Sarcoid Growths of the Skin, *J Cutan & Genito-Urin Dis* **19** 305-325, 1901.

12 Johnston, J. C. Fibrosarcoma Cutis, *J Cutan & Genito-Urin Dis* **21** 23-26, 1903.

13 Taylor, R. W. Sarcomatous Tumours Resembling in Some Respects Keloid, *J Cutan & Genito-Urin Dis* **8** 384-387, 1890.

14 Kartscher and Pfeiffer, cited by Hoffmann<sup>16</sup>.

made the diagnosis of desmoid, and this fact led Scmazzone<sup>15</sup> and McMaster<sup>4</sup> to believe that these cases were the first reported in the literature on the subject. Hoffmann<sup>16</sup> disagreed with this assumption. Senear, Andrews and Willis,<sup>17</sup> basing their arguments on Hoffmann's work, affirmed that Coenen<sup>18</sup> was the first to describe progressive and recurring dermatofibromas, in 1909. Favre and Josseland,<sup>1</sup> however, stated that the disease was known to Unna<sup>19</sup> in 1894. But on Nov 8, 1923, at a meeting of the French Society of Dermatology and Syphilography, Rabut and Cailliau<sup>20</sup> showed a case of fibroma of the abdominal wall. Darier<sup>21</sup> commented on this case, pointing out its importance and stating that he had already seen 2 cases. In 1924 Darier and Ferrand<sup>8</sup> made a study of 4 cases, 2 hitherto unpublished, 1 of Rabut and Cailliau<sup>20</sup> and 1 published on Feb 14, 1924. This was one of the most complete studies ever made of the subject, and the authors suggested for the morbid condition the name of progressive and recurring dermatofibroma or fibrosarcoma of the skin. Darier and Ferrand<sup>8</sup> expressed the belief that this new morbid entity had not yet been mentioned in the nosography of the subject. In strict justice to Darier and Ferrand it should be mentioned that it was only after their masterly and detailed description that this neoplasm became really known, as is shown by the greater number of cases published after 1924.

In 1925 Hoffmann,<sup>16</sup> in Germany, mentioned 3 cases and made a general review of the literature. He came to the conclusion that this disease was really first described in world medical literature by Coenen<sup>18</sup> in 1909 and that Kuznitzky and Grabisch<sup>22</sup> also wrote on the subject in 1921. Hoffmann<sup>16</sup> managed to get together 15 cases, including his own, reported in world medical literature up to the

15 Scmazzone, T. Contributo alla clinica e alla histologia dei fibrosarcomi cutanei, *Gior ital di dermat e sif* **67** 115-135, 1926.

16 Hoffmann, E. Ueber das knollentreibende Fibrosarkom der Haut, *Dermat Ztschr* **43** 1-28, 1925.

17 Senear, F. E., Andrews, E., and Willis, D. A. Progressive and Recurrent Dermatofibrosarcoma (Dermatofibrosarcoma Protuberans), *Arch Dermat & Syph* **17** 821-832 (June) 1928.

18 Coenen, H. Granulationsgeschwulste und Sarkome, *Beitr z klin Chir* **63** 337-346, 1909.

19 Unna, P. G. Die Histopathologie der Hautkrankheiten, Berlin, A. Hirschwald, 1894, *The Histopathology of the Diseases of the Skin*, translated by N. Walker, New York, The Macmillan Company, 1896.

20 Rabut, R., and Cailliau. Fibrome de la paroi abdominale, *Bull Soc franç de dermat et syph* **30** 392, 1923.

21 Darier, J., in discussion on Rabut and Cailliau<sup>20</sup>.

22 Kuznitzky, E., and Grabisch, A. Ueber myxomatose Fibrosarkome der vorderen Brustwand, *Arch f Dermat u Syph* **131** 23-32, 1921.

date of the publication of his paper in 1925. He also mentioned 6 other cases of tumors described in the literature on the subject as desmoid but which he presumed to be progressive recurring dermatofibroma. Senear, Andrews and Willis,<sup>17</sup> however, preferred not to take these cases into consideration in view of the deficiency of data and the uncertainty as to the true diagnosis. After the original paper of Darier and Ferrand,<sup>8</sup> in France, cases were reported by Touraine and Aubrun<sup>23</sup>, Gaté, Ricard, Guilleret and Moreau<sup>24</sup>, Chatelier<sup>25</sup>, Touraine and Payet<sup>26</sup>, Margarot, Plagniol and Guibert<sup>27</sup>, Darier<sup>28</sup>, Milian and Périn<sup>29</sup>, Pautrier and Woringer,<sup>30</sup> and Weissenbach, Thibaut, Martineau and Bouwens<sup>31</sup>. In Italy cases have been reported by Scolari,<sup>32</sup> Scmazzone,<sup>15</sup> Levi,<sup>33</sup> Pinetti,<sup>34</sup> Bertaccini<sup>35</sup> and Casazza<sup>36</sup>. In the United States cases have been reported by Senear, Andrews and Willis<sup>17</sup>, Weidman<sup>37</sup>, Binkley<sup>9</sup>, McMaster<sup>4</sup>, Michelson<sup>38</sup>, Taylor,<sup>13</sup>

23 Touraine, A, and Aubrun, W. Fibrosarcome tubereux de la peau de l'abdomen, *Bull Soc franç de dermat et syph* **40** 1689-1690, 1933

24 Gate, J, Ricard, A, Guilleret, P, and Moreau, P. Un cas de fibrosarcome de la peau, *Bull Soc franç de dermat et syph* **45** 162-165, 1938

25 Chatelier, M. L. Trois nouveaux cas de dermatofibromes tubereux de la peau, *Bull Soc franç de dermat et syph* **37** 608-610, 1930

26 Touraine, A, and Payet, M. Fibro-sarcome tubereux de l'abdomen, *Bull Soc franç de dermat et syph* **45** 1675-1677, 1938

27 Margarot, J, Plagniol, P, and Guibert, H. L. Dermatofibromes progressifs et récidivants (fibrosarcomes) de la paroi abdominale, *Bull Soc franç de dermat et syph* **38** 1156-1164, 1931

28 Darier, J. Un nouveau cas de fibrosarcomes de la peau, opéré et guéri, *Bull Soc franç de dermat et syph* **33** 32-36, 1926

29 Milian, G, and Perin, L. Fibro-sarcome au debut de la region malléolaire interne, *Bull Soc franç de dermat et syph* **33** 621-623, 1926

30 Pautrier, L. M, and Woringer, F. Dermato-fibrome progressif et récidivant de Darier-Ferrand, *Bull Soc franç de dermat et syph* **41** 611-617, 1934

31 Weissenbach, R. J, Thibaut, D, Martineau, J, and Bouwens, G. Tumeurs cutanées extensives de la region epigastrique évoluant depuis 25 ans (fibromes ou fibrosarcomes), *Bull Soc franç de dermat et syph* **45** 934-937, 1938

32 Scolari, E. G. Del fibrosarcoma cutaneo, *Gior ital di dermat e sif* **71** 1533-1558, 1930

33 Levi, I. Sopra un caso di fibrosarcoma primitivo delle cute del pene, *Gior ital di dermat e sif* **71** 1559-1574, 1930

34 Pinetti, P. Su di un caso di dermatofibroma progressivo recidivante di Darier a sede ed a struttura istopatologica non commune, *Gior ital di dermat e sif* **73** 811-820, 1932

35 Bertaccini, G. Fibro-sarcoma cutaneo primitivo in un bambino de cinque anni, *Arch ital di dermat, sif* **1** 1-9, 1925

36 Casazza, R. Osservazioni su un gruppo di non comuni casi di oncologia dermatologica, *Arch ital di dermat, sif* **8** 3-118, 1932

37 Weidman, F. D. Fibrosarcoma (?) of the Thigh, *Arch Dermat & Syph* **5** 421-422 (March) 1922

(Footnotes continued on next page)



and others. In Canada only 2 cases have been reported—by Usher<sup>39</sup>. In Argentina cases have been reported by Fidanza, Carrillo and Ocana<sup>7</sup>, Fernandez Blanco<sup>40</sup>, Alejandro and Bosq<sup>41</sup>, Puente and Copello,<sup>42</sup> and Seminario and Pessano<sup>43</sup>. In 1928 Kiess<sup>44</sup> observed another case and managed to get together 26 others already reported in world literature. Volk,<sup>45</sup> in 1928, in Vienna, and Nicolau,<sup>46</sup> in 1929 in Bucharest, reported 1 case each. In Brazil I have found records of only 1 published case, that of Fraga,<sup>47</sup> and accordingly, I believe mine to be the second case reported in this country. The diversity of opinion among different authors as to the chronologic order of the first cases published is due to the confusion which existed in the early stages resulting from insufficient and unsatisfactory clinical and histologic description and also from variations of nomenclature. Darier, Ferrand and Hoffmann corrected these deficiencies, giving to these interesting tumors a definite place in human pathology.

#### CLASSIFICATION

Before beginning the clinical description, it is indispensable to undertake the classification of these growths among the cutaneous tumors. As is known, the connective tissue is derived from the embryonic mesenchyma. In spite of the fact that this tissue is widely diffused in the organism, fibromas, with rare exceptions, are found only in the derma (dermatofibromas), the sheath of the musculus rectus abdominis (desmoid), the periosteum at the base of the cranium

38 Michelson, H. E. Dermatofibrosarcoma Protuberans, *Arch. Dermat. & Syph.* **25** 1127 (June) 1932.

39 Usher, B. Progressive and Recurrent Dermatofibrosarcoma (Dermatofibrosarcoma Protuberans), *Brit. J. Dermat.* **41** 363-369, 1929.

40 Fernandez Blanco, M. Consideraciones acerca de la histopatogenia de la enfermedad de Recklinghausen, *Semana med.* **2** 982-987, 1929.

41 Alejandro, S., and Bosq, P. J. Dermatofibroma de Darier, *Rev. argent. dermatosis* **22** 698-699, 1938.

42 Puente, J. J., and Copello, C. Dermatofibromas en la pared abdominal. *Rev. argent. dermatosis* **12** 152, 1927; Dermatofibroma en la pared abdominal. *Prensa med. argent.* **14** 575, 1927.

43 Seminario, C., and Pessano, J. Los dermatofibromas de Darier y Ferrand son formas frustradas de la enfermedad de Recklinghausen? *Rev. argent. dermatosis* **14** 61-69, 1930.

44 Kiess, O. Ein neuer Fall von Dermatofibrome progressif oder Fibrosarcome, *Dermat. Wchnschr.* **86** 1-7, 1928.

45 Volk. Fibrosarkom, *Dermat. Wchnschr.* **87** 1809, 1928.

46 Nicolau, S. Fibrosarkom der Bauchgegend, *Dermat. Wchnschr.* **89** 1342, 1929.

47 Fraga, A. Dermatofibromas progressivos recidivantes, *An. brasil. de dermat. sif.* **4** 69-71, 1933.

and of the long bones (basal and parosteal fibromas) and the ovarian stroma (ovarian fibromas). Of all these varieties the only ones that are of interest among those which occur in the derma are the progressive and recurring dermatofibromas which are connective neoplasms with a special clinical picture. Writers on the subject differ in their classification of these tumors as malignant or benign. This divergence of opinion is understandable, for it is not always easy to determine whether or not a cutaneous tumor is malignant. The histologic structure alone is not sufficient in all cases to determine malignancy, for the clinical behavior of the tumors is also of great importance. Eller<sup>48</sup> stated that progressive recurring dermatofibromas belong to the class of malignant tumors originating in the connective tissue. To the same group belong fibrosarcomas, myxosarcomas and liposarcomas, which constitute a variety of fibrosarcoma with a special clinical picture. Woringer<sup>6</sup> included them in the group of benign connective fibrocytic and histiocytic tumors along with the pastille fibroma of Civatte, the keloids and the muscular dissociating fibroma of the abdominal wall (desmoid), of the myxomas and of the histiocytomas. Favre and Josserand<sup>1</sup> included them among the malignant connective tissue tumors along with the other cutaneous sarcomas. As will be seen in the succeeding pages, progressive recurring dermatofibromas are really tumors which by their clinical and histologic characters may belong either to the malignant or to the benign group, of connective tissue neoplasms. Hence, in the classic examples of the growths one meets with characteristics which lead one to put them among the malignant connective tissue tumors, such a characteristic, for example, are resistance to treatment, tendency to recurrence and histologic features. But the elements which favor their non-malignancy are the absence of any effect on the general health, the absence of metastasis in most cases and their slow evolution. It is to be concluded therefore that these tumors, by their clinical and histologic characters, partake of the nature of both the malignant and the benign tumors, on the borderline of both. The criterion for judging whether or not such tumors are malignant is variable, because they show manifestations peculiar to both malignant and benign neoplasms, constituting a link between them and oscillating toward one side or the other as shown by the clinical cases so far observed. Bezecky<sup>3</sup> stated the belief that cutaneous fibrosarcoma is a diffuse fibromatosis due to hereditary predisposition which in its development gives rise to tumors. I am of the opinion that the hereditary factor does not seem to exercise any influence, for up to the present no case of familial involvement has been reported and most authors are of the same opinion.

<sup>48</sup> Eller J. J. Tumors of the Skin, Philadelphia, Lea & Febiger, 1939, p. 437

Binkley,<sup>9</sup> after studying 6 cases, expressed the idea that dermatofibrosarcoma, in spite of having definite clinical characteristics, is not different histologically from the other fibrosarcomas. Fidanza<sup>7</sup> asserted that, in his case at least, the growth was a fibroma, since no polymorphism, poikilochromia or cellular monstrosities were observed. He could not, however affirm that this tissue may not be transformed partially or totally into a sarcoma under influences which cannot be exactly defined. Fernandez Blanco,<sup>10</sup> in describing a case of cutaneous fibrosarcoma localized in the left inguinal region which began in infancy, expressed the belief that his patient, although not suffering from von Recklinghausen's disease, showed formations whose histologic features are those of the neurinomas encountered in this disease. This discovery made the author wonder whether he was not face to face with a case of abortive recurring von Recklinghausen's disease localized strictly in one region of the body. Seminario and Pessano,<sup>43</sup> also writing about a clinical case, wondered whether what is described as progressive recurring dermatofibroma or fibrosarcoma is not really an abortive form of von Recklinghausen's disease in process of transformation into sarcoma. Bobbio<sup>49</sup> affirmed that, according to his researches, dermatofibroma should be classified between desmoids and keloids, on the one side, and between the fibromas and fibrosarcomas, on the other.

#### DESCRIPTION

The symptoms of progressive recurring dermatofibromas are, with few exceptions, typical. The favorite sites are the abdomen and the inguinocrural region. The authors, though, can find no explanation for this preference except the histogenic theory of Binkley<sup>9</sup>. The localization of protuberant dermatofibrosarcomas, however, is not confined to the abdomen and inguinocrural regions but may be on any part of the cutaneous tegument (fig 1). Thus, they have been observed on the back, deltoid region, thighs, shoulders, dorsum of the foot, gluteal region, region of the kneecap, penis, malleolar region, wrist, face, submammary region, hairy scalp, etc. Localization on the head is rare, for up to the present only 4 cases with such localization have been reported. 2 on the hairy scalp and 2 on the face. In the former 2 cases, the sites of localization were the occipital region and the forehead and vertex. The tumor localized in the occipital region was observed by Yamasaki,<sup>50</sup> in Japan, and the one on the vertex and forehead was observed by me, in Brazil. The latter was the fourth one mentioned in world literature localized on the cephalic segment.

49 Bobbio, A. Tre casi de dermatofibroma, *Cancro* **2** 186-193, 1931.

50 Yamasaki, I. Zur Kenntnis des Dermatofibrosarcoma protuberans (E. Hoffmann) *Jap J Dermat & Urol* **43** 44-48, 1938.

and the second on the hairy scalp, it can thus be deduced that this localization is extremely rare. My case, indeed, is very similar to that of Yamasaki<sup>50</sup>. In typical cases of dermatofibrosarcoma the tumors are nearly always multiple, but single ones have been observed.

The shape of the tumor is variable: spherical, fungiform, pyriform, sessile, pedunculated, lobular, etc. The size varies from that of a peanut up to that of the head of a fetus. As regards the dimensions of the one in my case, I verified that it was one of the largest yet reported. The outlines or limits are always well defined, and the color varies, it may be violet red, pink or reddish. The surface may be smooth and uniform or eroded. When the surface of the tumor becomes eroded, it may turn red like a tomato and acquire a vegetative appearance. The excrescences are generally hard and cartilaginous but may become soft, especially when the surface becomes eroded. No liquid or secretory products are observed in the lesion, except when the surface becomes ulcerated. In most cases no changes in sensibility are observed. Involvement of lymph nodes has been reported in some cases but is not the rule, the enlargement must be regarded as being due to secondary infection and not to the tumor process itself. It is true that in the case of Levi<sup>33</sup> there was lymphatic metastasis, but this is the exception and not the general rule. It is well to emphasize at this point that progressive and recurring dermatofibroma, as described by Darier and Ferrand, presents a group of symptoms so typical and peculiar that certain cases, as I found in reviewing the world literature on the subject, differ so greatly from those described by the aforementioned authors that one is left in doubt as to the true diagnosis.

The evolution of a typical dermatofibrosarcoma takes place in two stages, the first of these consists of the formation of a fibrous plaque and the second is represented by the appearance of a tumor formation in this plaque. The period which elapses between stage one and stage two varies from case to case. The fibrous plaque may appear as such from the start or may be preceded by the appearance in the hypodermis of small hard infiltrating nodules which increase slowly in size and number and coalesce to form a pseudokeloid or sclerodermiform plaque which varies in size and may attain the dimensions of one's palm. The surface of the plaque is smooth and pale rose or dark in color and is hard to the touch, and the skin over it cannot be folded. The plaque is not attached to the subjacent tissues and can be made to slide over them. There are no subjective symptoms at this stage and the disease must not be confused with scleroderma. Some time, generally some years, after the plaque is fully formed, the tumor elements appear, and the last ones to form may attain an uncommonly large size in contrast with the slow growth of those which appear first. This is exactly what happened

in my case, in which the first tumors grew more slowly than the subsequent ones and much more so than those most recently formed

The description just given applies to the typical cases, but there are atypical ones. In Casazza's case,<sup>36</sup> for example, there was a limited zone of adherence to the deeper tissues. At times the surface of the plaque is not smooth but is studded with nodules, some of which are perceptible only on palpation while others are raised above the surface. In certain cases there is no stage of fibrous plaque formation, the disease begins with the appearance of one or more tumors. It is exactly those cases which differ from the classical clinical picture that need to be analyzed minutely both from the clinical point of view and from the histopathologic aspect in order to be classified with precision. In one of Fessler's<sup>51</sup> cases, for example, the clinical aspect of the fibrosarcoma was that of a fibroma, but the histologic examination showed transitional forms between fibroma and fusocellular sarcoma. Some cases, like the one reported by Nastase and Ionescu,<sup>52</sup> although conforming closely to the classical description of Darier and Ferrand, differ from it histologically by the presence of giant cells indicating a growth more malignant than fibrosarcoma. The neoplasm is restricted to the skin and hypodermis, but in some cases invasion of the underlying muscle has been observed. Lapa<sup>53</sup> affirmed that these tumors never ulcerate and stated that up to the time when his paper was written the appearance or spontaneous existence of this complication had never occurred. But in my case and in others there was ulceration. In some cases of fibrosarcoma the tumors are associated with other morbid manifestations, but this fact has no special pathologic importance. In the third case reported by Darier, for example, the cutaneous neoplasm was accompanied with a uterine fibroma. In the majority of cases pain is not mentioned as a symptom, but Senear<sup>17</sup> and Hoffmann<sup>16</sup> reported slight pain in some of the cases studied by them. Hemorrhage may supervene during the evolution of the tumors, and at the end there may be gangrene.

The question of the malignancy of these tumors is one that needs some attention. This question should be looked at from two points of view, the clinical and the histologic. From the former, fibrosarcoma behaves like a malignant tumor in that it is progressive, recurs when incompletely excised and can give rise to internal or cutaneous metastases. In most cases the evolution of the disease is slow. The tumors may remain stationary for a long time and then, later, without apparent cause

51 Fessler, A. Ein Fall von Dermatofibrosarcoma protuberans, *Dermat Ztschr* **72** 221-226, 1935

52 Nastase, G., and Ionescu, E. I. Fibro-sarcome ou dermatofibrome des cellules atypiques. *Bull Soc franç de dermat et syph* **43** 1529-1536, 1936

53 Lapa, A. Dermato-fibromas progressivos e recidivantes ou dermato-fibrosarcoma protuberans, *Lisboa med* **6** 355-376, 1929

or as a result of traumatism, begin to grow rapidly. The duration of the disease also varies from case to case, cases have been observed in which the disease lasted for fifteen, thirty-eight, forty-five and even as long as sixty years. No case of malignant sarcomatous change has yet been reported, except that of Alkiewicz.<sup>54</sup> Death generally occurs from some local or general intercurrent cause. Different authors have held different ideas about the possibility of the occurrence of metastasis. Darier<sup>8</sup> observed 1 case in which there appeared a cutaneous tumor far from the primary focus, but he stated that internal metastases are doubtful. Darier and Ferrand<sup>8</sup> expressed the belief that remote cutaneous metastases occur through the blood stream or at least the lymphatic channels. Usher<sup>39</sup> said that in his opinion the dissemination takes place by lymphatic channels but denied the existence of metastases to lymph nodes, which were observed by Levi.<sup>33</sup> Although internal metastases were reported by Bezecky,<sup>55</sup> Renzo,<sup>56</sup> Sciacchitano<sup>57</sup> and Binkley,<sup>9</sup> they are rare. The frequency of progressive recurring dermatofibroma is differently considered by different authors. Pinetti<sup>34</sup> in 1932 mentioned 40 cases reported, McMaster<sup>4</sup> in 1931 mentioned 39, and Ruiter<sup>58</sup> in 1934 cited 37. Woringer<sup>6</sup> in 1936 said that the disease was rare because up to that time only 35 cases had been reported in world medical literature. In 1938 Touraine and Payet<sup>26</sup> spoke of 50 published cases. Hertzler<sup>2</sup> reported 22 cases observed during twenty-five years of practice, but McMaster expressed the opinion that these tumors cannot be considered examples of progressive recurring dermatofibroma because they were capsulated and gave rise to metastases. Beck<sup>59</sup> in 1938 managed to catalogue 62 cases reported in world literature. In my search of the bibliography reviewing the subject, I found that 124 cases had been registered up to 1943, and of these I obtained the clinical summaries of 111. Sutton and Sutton<sup>60</sup>

54 Alkiewicz, J. Sur les rapports entre l'histiocytome et le dermatofibrome de Darier-Ferrand, *Rev franç de dermat et de venerol* **15** 195-210, 1939

55 Bezecky, R. Lungenmetastasen beim Dermatofibrosarcoma protuberans, *Arch f Dermat u Syph* **169** 347-353, 1933

56 Renzo, cited by Favre and Josserand<sup>1</sup>

57 Sciacchitano, G. Sopra un caso di fibro-sarcoma cutaneo con metastasi polmonari, *Tumori* **9** 427-438, 1935

58 Ruiter, M. Zwei Falle von progressiven und rezidivierenden Fibrosarcomen der Haut (Dermatofibrosarcoma protuberans), *Acta dermat-venerol* **17**: 162-170, 1936, *Dermatofibrosarcoma protuberans* *Nederl tijdschr v geneesk* **79** 4415, 1935

59 Beck, C. H. Zur Kenntnis des Dermatofibrosarcoma protuberans, *Arch f Dermat u Syph* **178** 260-268, 1938

60 Sutton, R. L. and Sutton, R. L., Jr. *Diseases of the Skin*, ed 10, St Louis, C. V. Mosby Company, 1939 p 775

stated that Geschickter and Lewis<sup>61</sup> observed 8 cases, in 7 of which the patients were women. Geschickter and Lewis' cases<sup>61</sup> were of simple dermatofibroma and not of protuberant dermatofibrosarcoma.

Summarizing his conclusions, Beck<sup>59</sup> stated that a case of dermatofibrosarcoma was described, the patient being a woman of 54 and the tumor being situated in the abdomen. The morbid picture of dermatofibrosarcoma protuberans was completed from the data of 63 cases described. In this way the following conclusions were derived:

- 1 This disease occurs with the same frequency in the two sexes.
- 2 The favorite sites of the disease are the abdomen, thorax, lower limbs, back, inguinal fold and upper limbs.
- 3 In 75 per cent of cases the tumor had already existed for five years before the beginning of treatment, while in 19 per cent the disease had existed for twenty-six years or more.
- 4 The first manifestations occurred in a small percentage of cases before the patient's twenty-sixth birthday, while in 11 per cent these first symptoms appeared before the age of 6. In more than half the cases treatment was begun between the ages of 36 and 55.
- 5 Dermatofibrosarcoma protuberans of the thorax shows a greater tendency to myxomatous degeneration than that on any other part of the body.
- 6 The older the tumor, the more frequent the occurrence of myxomatous degeneration is.
- 7 It is not yet possible to form an idea of the possible malignancy of a dermatofibrosarcoma either by its age or by its histologic structure, although hitherto more signs of malignancy have been discovered in cases with myxomatous degeneration than in others.
- 8 It is probable that, in spite of all, the tumors described by Hertzler are examples of dermatofibrosarcoma protuberans.

#### RACES

Dermatofibrosarcoma has been found in nearly all races—the white, the yellow and the black. My case and that of Fraga<sup>47</sup> constitute the first ones reported in world literature as occurring in brown mestizos (mulattoes). The largest number of cases have occurred among white persons, followed by black persons, Asiatics and mestizos in that order.

#### SUBSIDIARY TESTS

The laboratory diagnosis of progressive recurring dermatofibrosarcoma rests on the anatomicopathologic examination. For this purpose fragments for biopsy are taken in accordance with the rules already

<sup>61</sup> Geschickter, C. F., and Lewis, D. Tumors of Connective Tissue, *Am J Cancer* **25** 630-655, 1935.

laid down for this purpose. It is advisable, however, that they be taken from various parts of the tumor elements so as to obtain specimens of the various evolutionary phases, that is to say, different structural aspects, as happens in certain cases. Some authors have reported positive Wassermann reactions in certain cases, but this shows only that the patients were suffering from syphilis and not that their respective cutaneous lesions were of syphilitic origin, this is borne out by the inefficacy of syphilitic treatment in these cases. My case constituted a good example of this for the Wassermann reaction was positive but antisyphilitic treatment had no influence on the course of the cutaneous lesions.

#### PATHOLOGIC ANATOMY

I shall divide the pathologic anatomy into two parts: one part dealing with the structural changes found by various authors and the other the study of the preparations obtained by me in the case which is dealt with in this paper. Generally speaking, the pathologic anatomy of progressive recurring dermatofibrosarcoma is not very different from that given in the classic description of Darier and Ferrand,<sup>8</sup> but there are circumstances in which some abnormality occurs. Pautrier and Woringer<sup>62</sup> found, in 1 case, small nerves and isolated nerve filaments running through the interior of fibromatous bundles. However, sections made in series and the topographic layout showed that these were nerve endings around a hair follicle which had already disappeared as well as of remains of nerves which had resisted the destructive action of the tumor substance. Fatty infiltration and myxomatous degeneration have already been mentioned. It has been found that old tumors are more fibrous and the more recent ones are richer in cells. The capsule found by Hertzler<sup>2</sup> in his cases has not been mentioned by the majority of authors who have studied the subject. Favre and Josserand,<sup>1</sup> however, stated that some authors refer to a well defined capsule but affirm that the presence of such elements is not important, since capsulated fibrosarcomas have already been observed. According to Favre and Josserand,<sup>1</sup> the differentiated skin structures, such as nerves, glands and hair, disappear on account of the infiltration, but there have been cases in which the smooth muscles remain intact and in which the sweat glands persist, dissociated or encysted. Atypical cellular and karyokinetic forms have been observed. Margarot<sup>27</sup> and Pinetti<sup>34</sup> observed cases in which the vascular formations were so well developed that it was possible to refer to the tumors as angio-fibromas and angiosarcomas. Besides such changes, there are also mentioned necrotic areas, sclerosis of the vascular walls and obliteration.

<sup>62</sup> Pautrier, L. M., and Woringer, F. *Dermat-fibrome de Darier-Ferrand*, Bull. Soc. franç. de dermat. et syph. **44**: 2171-2174, 1937.



tion of the lumen of the blood vessels by endovascular proliferation. As regards my case, I selected for biopsy three fragments of tumors in different stages of evolution. I shall, however, describe only one of these and make a general interpretation of the histologic changes met with in all three. The histologic description of my preparations is as follows:

**SPECIMEN 1**—The whole surface of the preparation was ulcerated showing a relatively extensive area covered with a fibrinopurulent exudate, the superficial layers of which were infiltrated by polymorphonuclear neutrophils, plasma cells and lymphocytes, one or other of these inflammatory cells predominating according to the area. It must be borne in mind also that the vascularization is distinctly more pronounced in the upper than in the deep layers, there being present in the superficial layers numerous new blood vessels some of them showing dilatation of their lumen. This superficial zone is therefore represented by true granulation tissue. Below this granulation tissue and prolonging it insensibly, there is a connective tissue neoplasm fasciculated in structure (fig 1 *A*), with bands of tissue crossing each other in the most varied manner, now transversally, now obliquely and even at times in a kind of whorl. As regards cytology, the tumor is found to consist of fusiform cells, with nuclei of varying size, some being long and thin and others shorter and thicker, the former are more hyperchromatic than the latter. These nuclei generally contain one or two nucleoli, and the protoplasm has indistinct borders. A fibrillary intercellular substance is distinctly visible (fig 1 *B*). When stained by Van Gieson's method these fibrillae do not stain with fuchsin, but with Mallory's stain for collagen they are stained blue. There are no elastic fibers (Rubens Duval method). No karyokinetic figures were found, but a small number of atypical cells were met. The majority of the blood vessels are lined only with endothelium. In some of them, however, the other lining tissues are met. There is neither myxomatous degeneration nor fatty infiltration.

#### INTERPRETATION OF THE HISTOLOGIC CHANGES

According to Moacu Junquiera, the histologic changes in the specimens which were taken at the levels of the different tumors showed that the structure of the tumors was about the same, for all of them were connective tissue neoplasms consisting of strands which crossed each other in different directions and which were built up of elongated cells that showed practically no pleomorphism apart from a few atypical forms which were not seen, however, in all of the blastomas. The absence in all of them of karyokinesis, either typical or atypical, must be emphasized. In some preparations the dividing line between the neoplasm and the superficial derma could be observed, but no capsular formation was to be seen. Only one of the tumors was ulcerated, but in the parenchyma itself in no case was there observed any necrotic area or any form of degenerative change. From all these facts it can be concluded that I was really dealing with cases of dermatofibroma because no elements were met indicating evident histologic malignancy,



Fig 1—*A*, section showing the fasciculated structure and the varied direction of the connective tissue strands *B*, preparation showing the greater abundance of the intercellular collagen

there were therefore no grounds for classifying the tumors as fibrosarcomas or fibroblastic sarcomas

It must be borne in mind, however, that, as can be deduced from the histologic description of the cases of different authors, these neoplasms do not present a characteristic and unchanging histopathologic structure, this on the contrary varies according to circumstances. The final diagnosis, therefore, must be based rather on the clinical symptoms than on the laboratory examination. The histologic examination serves as a complement to the clinical examination.

#### DIFFERENTIAL DIAGNOSIS

The differential diagnosis must be made between this disease and benign connective tissue fibrocytic or histiocytic tumors, malignant connective tissue tumors, von Recklinghausen's disease, simple pedunculated fibroma and patchy scleroderma. Among benign fibrocytic connective tissue neoplasms are included fibromatoses and fibromas properly so-called. In my case chiefly and in that of Yamasaki,<sup>50</sup> on account of the exceptional localization on the hairy scalp, it is necessary in making the differential diagnosis to bear in mind the possibility of confusion with the wens of this region and with the cylindromas, which are tumors called by the English "turban tumors", many illustrative cases of these are to be found in the excellent work of Ronchese.<sup>63</sup>

#### HISTOGENIC THEORIES

Various theories have been formulated to explain the histogenesis. Binkley<sup>9</sup> stated

Because of the unusual predilection of dermatofibrosarcoma for the anterior surface of the body to the right and left of the midline, a possible embryologic relation to the mammary ridge suggested itself. To test this theory, a spot map (fig 2) was made showing the situations of the tumors thus far reported. This showed at once that these tumors occur with remarkable frequency at or near the mammary ridge. Many of them are situated on the neck, above the clavicle, and also on the upper part of the chest above or below the breast. On the abdominal wall, they are usually in the lower quadrants several centimeters to the right or left of the umbilicus. The growths occur frequently in the groin and occasionally on the medial side of the superior portion of the thigh. A few tumors have been observed on the back, on the buttocks and on the extremities, and one was on the penis.

Wiedersheim, along with other embryologists, has stated that "in the great group of Carnivora and in the pigs, the teats are arranged in two rows converging toward the pelvic region." Pinkus stated that "the mammary ridge in young embryos is sometimes seen extending over the dorsum and down to the caudal region." This fact would explain the situation of some tumors on the back or

<sup>63</sup> Ronchese, F. Multiple Benign Epithelioma of the Scalp (Turban Tumors), *Am J Cancer* **18** 875-887, 1933.

on the buttocks, usually a few centimeters to the right or left of the midline. The theory that dermatofibrosarcomas originate from the mammary ridge explains the multiple skin tumors without metastases observed by Darier and Ferrand, Coenen, Willis, Usher and Bezecky. It is difficult by this theory of origin, to account for the tumors which have been observed on the wrist and on the penis. They apparently were dermatofibrosarcomas without relation to the mammary ridge, unless they could be accounted for on the basis of aberrant embryonic tissue in these situations.

Mosto,<sup>5</sup> studying preparations made in a case of dermatofibrosarcoma observed by Seminario and Pessano,<sup>43</sup> expressed disagreement with the opinion of Darier and Ferrand, who attributed a mesenchymal and therefore connective tissue origin to this neoplasm.

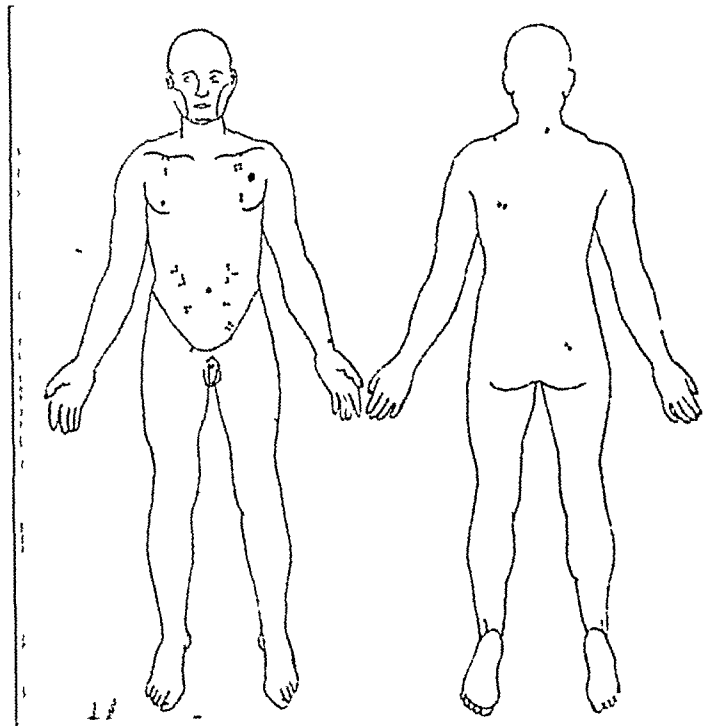


Fig 2—Spot map showing the situation of dermatofibrosarcoma protuberans in reported cases. The distribution suggests a relation to the mammary ridge (Binkley)

which participates at the same time of the nature of fibroma and of a sarcoma. He expressed the opinion that histologically progressive and recurrent dermatofibroma is not identical with fusocellular or fibroblastic sarcoma, for its histopathologic picture does not show the structural elements peculiar to the latter. According to Mosto,<sup>5</sup> the arrangement of the fine strands oriented in multiple directions which are shown in different sections made in the most varied positions makes one at first sight think of a plexiform neuroma. As a matter of fact, this plexiform arrangement is rare in purely connective tissue tumors, which show a coarser network with a larger amount of collagen and disappearance of nuclei forming subsequently thick connective tissue.

strands which rapidly become hyalinized. This form of network formed by fine strands whose branches are in intimate relation with one another, constituting as it were, beams interspersed with small filaments, evidently corresponds to the peripheral neuromas. On the other hand, there can also be adduced in favor of this opinion the characteristic palisade arrangement of numerous fibrillae and also the alinement at certain spots of chains of cells. The definite separation of the obviously collagenous connective tissue from the nerve-like-appearing fibrillae presents a vivid contrast in certain areas. This can be affirmed categorically after differential staining for Van Gieson's stain produces not a reddish but a frankly yellowish color. Mallory's phosphotungstic acid hematoxylin produces a light blue color in certain areas and a darker blue in others. With the aid of Del Rio Ortega's ammoniated carbonate of silver, splendid impregnations of nerve substrate can be obtained. In such a case neither neurites nor myelin sheaths are observed, hence the type corresponds to that of aneuritic neuroma or peripheral glioma. These tumors, by autonomous proliferation of neuroglia cells or of Schwann's sheath, give rise later, like connective tissue cells, to collagenous substance. That is to say, these tumors consist of pure neuroglia and secondarily of well vascularized connective tissue and numerous capillaries, some of them embedded in collagen. Therefore one should consider them not as fibromas or dermatofibromas but as dermatoneuromas or rather as dermatoschwannomas or peripheral dermatogliomas with some structural resemblance to the dermal tumors of von Recklinghausen. Darier,<sup>64</sup> however, did not contest the clinical diagnosis or the microscopic structure in Seminario and Pessano's<sup>43</sup> case which Mosto<sup>5</sup> studied histopathologically, for it fits in perfectly with the clinical and histologic characteristics of progressive and recurrent dermatofibroma. As regards the origin of this neoplasm, Darier<sup>64</sup> took up a point of view opposed to that of Mosto,<sup>5</sup> alleging that the arguments in favor of the neuritic or gliomatous theory of origin of these tumors are not convincing. Mosto's<sup>5</sup> theory also has been contested by Pautrier and Woringer<sup>62</sup> and by Scolari.<sup>32</sup> Mosto<sup>5</sup> indeed drew hasty conclusions, especially since this is a matter which requires deep study and long reflection before any definite opinion can be formed. It must be added that recently Bogliolo<sup>65</sup> corroborating the opinion of Penfield<sup>60</sup> Bailey and Hermann,<sup>66</sup> Parker,<sup>66</sup> Adison and Kermohan<sup>66</sup> and Ewing,<sup>66</sup> said

64 Darier, J. Les fibrosarcomes de la peau sont-ils des dermatoneuromes? *Ann de dermat et syph* 10 852-855, 1929

65 Bogliolo, L. Os assim chamados neurinomas (angio-fibro-blastomas, fibro-blastomas), com especial referencia aos do angulo ponto-cerebelar, *Resenha clin-cient* 12 227-234, 1943

66 Cited by Bogliolo<sup>65</sup>

the neurinomas are blastomas of a connective tissue nature and consequently of mesenchymal origin. This theory is opposed to that of Mosto,<sup>5</sup> who attributes to such tumors an ectodermic origin. Alkiewicz,<sup>54</sup> basing his opinion on the work of Civatte<sup>67</sup> on the relations between histiocytoma and lozenge-shaped fibroma and guided also by his observation of a case in which there existed side by side lesions of the Darier and Ferrand dermatofibroma type of histiocytoma, concluded that the "histiocyte is a temporary evolutionary form which later becomes a fibroblast. So histiocytoma can finally evolve into a fibroma. Contrary to the opinion generally held so far, there may originate from it not only a lozenge-shaped fibroma but also a Darier-Ferrand dermatofibroma, and so the latter may at times be a histiocytoma which has undergone cure." Alkiewicz<sup>54</sup> admitted that in the same way that the lozenge-shaped fibroma springs from a histiocytoma the latter can also give rise to progressive recurrent dermatofibroma, as happened in his case, in which there was also evident evolution of the dermatofibroma into sarcoma. After an examination of the preparations, Civatte<sup>67</sup> concurred in this opinion. Favre and Josserand,<sup>1</sup> however, expressed the belief that the ideas about connective tissue tumors and the formations which one calls sarcomas are oversimplified and rudimentary, they stated that dermatologists ought therefore to limit themselves, for the time being, to affirming the existence of cutaneous connective tissue neoplasms which show an evident contrast between histologic malignancy and a clinically benign character as is the case with certain cutaneous neoplasms of epithelial origin. The attempts made to explain the intimate mechanism of the formation of progressive and recurrent dermatofibromas represent so far only a simple effort on the part of research workers to elucidate the unknown factors of this neoplasm as occurs with blastomas in general.

#### ETIOLOGY

The cause of progressive and recurrent dermatofibromas is unknown. In the great majority of cases these tumors appear without the slightest apparent cause. It is true that some authors have mentioned as a starting point an old surgical scar, nevus and even, in 1 case, a scar of lupus. But these theories give no help in unraveling the unknown cause of the curious tumors being studied. It may however be asked whether the scar or even the nevus constituted a weak spot of lessened resistance or functioned as an irritant and thus facilitated the occurrence of the dermatofibroma. Several authors have also reported the appearance of these cutaneous fibrosarcomas in areas exposed to previous traumatism but they said that this factor played no part in the

<sup>67</sup> Civatte cited by Alkiewicz.<sup>54</sup>

occurrence of the tumor. In my case the traumatism of the forehead and crown of the head continued for a long time with relatively great intensity because the patient was in the habit of carrying various objects on the head, as is the habit among the rural populace in Brazil. I believe that in those cases at least in which previous traumatism exists the traumatic element can be invoked to explain the start of the disease, not as an effective cause but as an adventitious or secondary one by setting up a zone of lowered resistance, thus favoring the appearance of the neoplasm. The part played by traumatism in the localization of syphilis in certain cases is well known as well as in the origin of certain cases of leprosy and even in the predilection of blastomas for organic sectors subjected to repeated traumatism.

#### PROGNOSIS

The prognosis of progressive and recurrent dermatofibroma is more unfavorable than that of simple fibroma because of the resistance of the former to treatment and its tendency to continuous progression and recurrence, there may even be metastases. But the prognosis is incomparably less serious than it is for sarcoma. Early treatment well carried out has a decisive influence on the prognosis.

#### PROPHYLAXIS

It has not been possible to carry out efficiently the prophylaxis of progressive and recurrent dermatofibroma.

#### TREATMENT

The most varied forms of treatment have already been adopted for protuberant dermatofibrosarcoma. Radium therapy has been employed as well as radiotherapy, electrocoagulation, surgical excision, coagulation and excision with previous and subsequent radiotherapy. Darier<sup>8</sup> stated the belief that no form of treatment can prevent the progressive development of this tumor, except ample and early surgical removal. Usher<sup>39</sup> said that he thought that dermatofibrosarcoma resists all forms of treatment except ample removal of the tumor mass. The conclusion I have arrived at as regards the different methods of treatment employed in the cases which I have been able to study is that wide surgical removal with subsequent radiotherapy constitutes the method to be preferred. But the excision should go beyond the limits of the neoplasm and partly attain the sound tissues. The most frequent cause of recurrence is inadequate excision. When there is a sclerodermatous plaque, it should also be excised entire with inclusion of the tissues a little beyond its border. In my case I could not employ adequate treatment, because the patient would not consent to the total surgical removal of the tumors and of the fibrous plaque.

## REPORT OF A CASE

O A S, aged 38, a Brazilian Negro farmer, born at Dolores de Guanhanes, State of Minas Geraes, residing at Baraunas was an inpatient at the Radium Institute (Director, Prof Borges da Costa) under the care of Dr Alysson de Abreu

*Family History*—The father died at 80 of a cause unknown to the patient. The mother was alive and strong at 60. She never had abortions and had nine full time pregnancies. Four children were alive and strong, and four died in early infancy of causes unknown to the patient. His relatives were healthy. There was no case of a disease similar to his in a member of his family.

*Personal History*—(a) *Physiologic* The patient smokes and drinks and is a great coffee drinker. He is a field worker and exposed therefore to all kinds of weather. His nourishment has been deficient.

(b) *Pathologic* He said that he had had grip, malaria, worms, gonococcic urethritis and mixed chancres.

(c) *Previous Operations* He was operated on five years previously for tumors on the hairy scalp.

*History of the Present Disease*—The patient said that about six years previously, in 1938, he noticed a thickening of the hairy scalp over the forehead and crown of the head. This thickening had the appearance of a callosity and in his opinion was due to carrying heavy objects on the head. Subsequently, after a period which he could not exactly determine, there appeared on the fibrous plaque in the center of the right frontoparietal region a small tumor which continued to grow until 1939, when he had it removed by a surgeon in the Bello Horizonte Public Hospital. One year later another nodule appeared on the scar, and several others presented themselves round the site of the original nodule, all were small, except the one in the left frontal region, which grew to the size of a tangerine (fig 3). There were no subjective symptoms. In November 1940 the patient went to the Radium Institute in this city where he was subjected to various tests, including the Wassermann, to which the reaction was positive (4 plus). It was therefore thought that his lesions were of syphilitic origin, but the specific treatment was ineffective. In July 1941 he returned home, after refusing to have the tumors removed surgically. On April 3, 1943 he returned to the Radium Institute and stated that toward the end of 1942 one of the small nodules on the right frontoparietal region had begun to grow rapidly, attaining the size of the head of a fetus. The tumor sprouted a stalk, became eroded and fell over the right eye and right side of the face (fig 4). The nodule on the left frontal region also increased in size, becoming bosselated. The patient complained of pain and weakness, affirming that he could not see with the right eye because the large tumor formation falling over his face obstructed his vision.

*General Examination*—The facial appearance was normal and the attitude active. There was lateral inclination of the head toward the left as this prevents traction on the stalk of the largest tumor and so eases the patient. The nails and hair were normal, except for loss of hair on those parts of the scalp in which there was tumor growth. *Skin* There were scars left by dental fistulas on the left lower maxillary region and by ulcerated adenitis in the right groin. The skin was brown and dry and moved freely. Over the level of the forehead and crown of the head there were twenty tumors, three of which were large, the others being about the size of a hazelnut. Two of the three large tumors were situated in the right temporoparietofrontal region and the other in the corresponding



region on the left. Of the two tumors on the right one was farther forward, spreading toward the frontal region, and the other was nearer the intersection of the temporal and parietal regions. The frontal tumor was unusually large and was pedunculated, falling over the upper two thirds of the right side of the



Fig 3—Progressive and recurrent dermatofibroma of Darier and Ferrand. Rare implantation on the hairy scalp (in 1940)



Fig 4—Progressive and recurrent dermatofibroma of Darier and Ferrand

face and totally covering the corresponding orbital region. This large tumor was circular in outline, the size of the head of a fetus, pink and measuring 14 by 17 cm, with its outer surface eroded in part and secreting a yellowish foul-smelling liquid. There were crusts which were hard to the touch. The tumor

was painless, and its surface was irregular in part and partly smooth. There was intense vascularity. The tumor was joined to the frontal region by a stalk covered with smooth, freely movable skin, which could be taken up in folds by the fingers. As the stalk was appreciably long, the large tumor mass could be raised so as to uncover the upper two thirds of the face and the orbital region. (The eyeball was in perfect condition.) It should be pointed out that it was only by so doing that the patient could use his right eye. Palpation of the stalk showed that it consisted of a hard wide fibrous cord, which was greatly stretched by the tumor. The internal surface of this tumor was smooth and concave. The skin over the tumor itself could not be taken up in folds. The second tumor, which was smaller, the size of a tangerine, was situated behind the first, with which it was confluent at its base. It was bosselated and sessile, pink, hard to the touch and eroded on the surface. The third of the three larger tumors was 6 by 5 cm and was situated on the left side of the frontal region, hard to the touch and with an irregular bosselated surface, eroded at certain points, sessile and pink and had another excrescence on its surface. The other tumors, which were smaller than these three, showed on a smaller scale the same clinical features and were also painless. All the tumors—that is, the ones on the crown and forehead—rested on a sclerodermiform plaque which was hard, smooth and hairless at certain points and did not move over the underlying tissues. Some tumors merely appeared at the surface of the plaque.

**Visible Mucosae** The visible mucosae were normal in color. The musculature was of good tonicity and the subcutaneous cellular tissue normal. The patient had a temperature of 36.5 C [97.7 F], was 172 cm tall and weighed 51 kilograms. Examination revealed that the respiratory, circulatory and digestive systems, the liver and the urogenital apparatus were normal.

**Lymphohemopoietic Apparatus** The epitrochlear and inguinal lymph nodes were enlarged. The spleen was not perceptible on palpation. The locomotor apparatus and the nervous system were normal. A complementary examination gave a positive (4 plus) Wassermann reaction.

#### SUMMARY AND CONCLUSIONS

The clinical report of a case of progressive and recurrent dermatofibroma (of Darier and Ferrand), the second case reported in Brazil is made. There exist various synonyms for this cutaneous affection, but the name of progressive and recurrent dermatofibroma should be adopted in honor of Darier and Ferrand. The first cases of this clinical condition were described by Taylor and Sherwell in 1890 in the United States, but it was Darier, along with Ferrand and Hoffman, who gave it a definite place in human pathology. These tumors should be classified between the fibromas and the sarcomas oscillating toward one or the other class according to the case. The classic clinical symptoms are characteristic but in atypical cases careful interpretation of symptoms is needed for correct classification. Progressive and recurrent dermatofibromas can occur on any part of the skin but the hairy scalp, face and penis are rare sites. In the cases hitherto reported members of the two sexes were unequally attacked there being a visible predominance of the disease among males. Up to 1943 124 cases

(not including Hertzler's 22 cases) had been reported in world medical literature, hence the disease can no longer be considered extremely rare, as was formerly believed to be the case. The races attacked in the descending order are the white, the black, the yellow and the mixed. This neoplasm is of mesenchymal and therefore of connective tissue origin. The differential diagnosis must be made between this disease and localized scleroderma, keloid, Civatte's lozenge-shaped fibroma, histiocytoma and myxoma, fungoid mycosis, desmoid of the abdominal wall, von Recklinghausen's disease, Perrin's and Kaposi's sarcomatosis and other cutaneous sarcomas. In my case and in that of Yamasaki the differential diagnosis had also to be made between it and wen of the hairy scalp and the tumors called "turban tumors" by the English. The cause is unknown. The prognosis is more serious than that of fibromas but less serious than that of cutaneous sarcomas properly so-called. On account of ignorance of the cause, prophylaxis cannot be carried out. As regards the tumor in question, histopathologic examination showed it to be a dermatofibroma. The positive diagnosis of this neoplasm is clinical rather than anatomicopathologic, for these blastomas do not present characteristic and unchanging histopathologic features, these, on the contrary, vary from case to case and according to the stage of evolution of the morbid process. The best treatment is total wide excision of the tumors and of the fibrous plaque (when this is present) followed by radiotherapy.

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# Clinical Notes

## KERATOSIS BLENORRHAGICA

GERALD A. SPENCER, M.D., NEW YORK

Cutaneous manifestations of gonorrheal infection are not a common occurrence. Now that the era of sulfonamide and penicillin medications is being passed through, gonorrheal dermatosis will in time become a still rarer observation. The case of keratosis blenorragica reported in this paper is of interest because it presented three unusual features. First, the clinical appearance of the infection was not the usual type. Second, the condition occurred in a woman, in whom it is not frequently encountered. Third, there was the early response to sulfonamide medication and rapid involution of the cutaneous lesion.



Fig 1—4, thickening and cracking of soles. B, complete healing of lesions on soles.

### REPORT OF A CASE

H. V., a woman aged 38, complained of an eruption on the palms and soles, which extended to the legs. The onset of the disease began two months previously, when she first noticed a thickening and cracking of the soles and palms, and then a rash appeared on the legs and forearms.

Examination showed a diffuse thickening and cracking of the soles (fig 1, 2), which made walking difficult. On the legs there were discrete and confluent papulosquamous lesions that extended to the knees. Some of the new or papular

lesions were soft and hemorrhagic. On the palms there was a diffuse thickening, chiefly situated on the central portion, with discrete papular lesions on the borders, which thickening extended to the anterior aspect of both wrists. There were no lesions on the other portions of the cutaneous surface.

The patient denied having had syphilis or ever having received antisyphilitic medication. Further interrogation revealed that she had taken no medicaments by mouth or parenterally.

Genital examination showed that there was a profuse mucopurulent vaginal discharge. Specimens for smear and cultural examinations were obtained from the urethra and the cervix. Cultures were reported positive for gram-negative diplococci.

The Wassermann reaction of the blood was negative. No abnormalities were found in the urine. The physical examination showed no other abnormalities.

The patient then was given sulfathiazole medication, in doses of 1 Gm tablets, to be taken every four hours for ten days. Four weeks later additional specimens for smear and cultural examinations were reported negative. At this time, the lesions on the legs had completely disappeared and the thickening of the palms and soles was considerably reduced. Two months later the palms and soles were completely free of lesions (fig 1 B).

#### SUMMARY

A case of keratosis blenorrhagica in a woman with unusual clinical manifestations is reported.

Diagnosis was confirmed by cultural studies of material from two genital foci.

Treatment with sulfathiazole taken internally in adequate dosage brought about speedy cure of the infection, with rapid involution of the cutaneous lesions.

129 West One Hundred and Twenty-Ninth Street

#### THE USE OF VIOFORM IN LOCAL DERMATOLOGIC THERAPY

THOMAS S. SAUNDERS, M.D., PORTLAND, ORE

In a footnote in their book entitled "Dermatologic Therapy in General Practice," Sulzberger and Wolf<sup>1</sup> have stated that "this local remedy [Vioform, 1 to 3 per cent in petrolatum] is unfortunately not sufficiently appreciated." On the basis of extensive clinical trial, it proved to be "one of the best antieczematous, mildly soothing and antiparasitic remedies."

Not wishing to deprive my patients of such an apparently valuable remedy, I prescribed it to several suffering from superficial inflammatory diseases of the skin (eczema, tinea, eczematized dermatophytosis, eczematoid dermatitis and others). To minimize the possibility of irritation, 1 per cent of the drug in petrolatum was used. In 14 cases, the results were definitely known. The patients in 5 of these were cured either by the ointment or some measure used simultaneously, such as the avoidance of suspected contact allergens. In 5 others the disease was unaffected by the salve, and in 4 other cases the eruption became worse, apparently aggravated by the ointment.

Because the incidence of irritation was too high and the proportion of beneficial results was too low, further study of the medication was not attempted.

1020 South West Taylor Street

<sup>1</sup> Sulzberger, M. D., and Wolf, J. *Dermatologic Therapy in General Practice*, ed 2, Chicago, The Year Book Publishers, Inc., 1942, p. 106.

## Obituaries

### MIHRAN BOGHOS PAROUNAGIAN, M D

1874-1946

Mihran Boghos Parounagian died of a heart attack at his country place in Cornwall on the Hudson, N Y , on June 13, 1946

Dr Parounagian, the son of a blacksmith, was born in Caesarea, Armenia, on July 10, 1874. He migrated to the United States as a boy and after receiving his preliminary education entered New York University College of Medicine, he received his degree in medicine in 1895. He entered active practice after interning for a year at the Almshouse and Workhouse Hospital on Welfare Island, New York city. His early interest in dermatology and syphilology brought him into close contact with the masters of his generation, H G Piffard, J A Fordyce and S Pollitzer, whose tutelage and friendship he enjoyed. Dr Parounagian was appointed instructor and then adjunct professor of dermatology and syphilology at the New York Post-Graduate Medical School and Hospital (1906 to 1916). He was visiting dermatologist to City Hospital, beginning in 1906. He never relinquished his several associations with the departments of dermatology and syphilis of the hospital system of New York. He held positions as chief of dermatology and syphilology at Gouverneur Hospital from 1910 to 1919, continuing from that time as consultant, and as visiting dermatologist and syphilologist at Bellevue Hospital and chief of the outpatient department of that institution from 1918 to 1936, after which he maintained his affiliation as a consultant. Dr Parounagian was acting professor of dermatology at the University of Vermont College of Medicine in 1918 and clinical professor of dermatology and syphilology at New York University College of Medicine, beginning in 1929. The list of consulting posts included St Luke's Hospital, Newburgh N Y, St Francis Hospital, Poughkeepsie, N Y, Medical Center of Jersey City, Jersey City N J, Manhattan State Hospital New York, Cornwall Hospital Cornwall N Y, Tuxedo Memorial Hospital Tuxedo Park N Y and Bayonne Hospital and Dispensary Bayonne N J.

Dr Parounagian was a member of the American Medical Association, fellow of the New York Academy of Medicine, member of the Manhattan Dermatologic Society and president and founder of the Armenian Medical Society. He was active in these societies holding chairmanship in the Armenian Medical Society from 1933 to 1936 and again from 1938 to the date of his death. He was chairman of the New

York Academy of Medicine, Section of Dermatology and Syphilis, from 1926 to 1927 and was president of the Manhattan Dermatologic Society for several terms, being one of the earliest members of this society



MIHRAN BOGHOS PAROUNAGIAN

1874-1946

Dr Parounagian enjoyed a large circle of friends. He was tenacious in holding his friends to him. Classmates were happy to be listed among his friends over half a century after graduation. He was

a friend of his patients. He courageously fought for improved clinic facilities and made his influential friends understand his passion for the need and advance of hospital and clinical aid to the ill.

Dr. Parounagian demonstrated his theories by presenting many patients before the New York Academy of Medicine, Section of Dermatology and Syphilis, and the Manhattan Dermatologic Society. He was intense in discussion, drawing on his own experiences rather than referring to the literature of the past.

Dr. Parounagian married Sophie Phoebe Freudenburg on June 7, 1895. She survives him. Having no children, the couple devoted themselves to the children of close relatives. After a coronary incident in 1936, Dr. Parounagian curbed his professional activities at office and hospital and spent more time at his country place in Cornwall on the Hudson, N. Y.

V. BOGHOSIAN, M.D.

## News and Comment

**American Board of Dermatology and Syphilology**—At the recent meeting of the American Board of Dermatology and Syphilology held in San Francisco, June 28 and 29, the following thirty-nine candidates were granted certificates by the Board and may now be referred to as diplomates: Jacob Bleiberg, Newark, N. J.; Alexander M. Buchholz, Chicago; Paul Joseph Catinella, Rochester, Minn.; Harry A. Cumming, Minneapolis; Werner Duemling, San Diego, Calif.; Emanuel Montague Famer, Los Angeles; Gerald Myron Frumess, Denver; Solomon Greenberg, Bayonne, N. J.; Moses Henry Holland, Weehawken, N. J.; Alfred Hollander, Springfield, Mass.; Alfred H. Illge, Portland, Ore.; Stanley James Joyce, Detroit; Ben Kance, Vancouver, British Columbia, Canada; George Kien, New York; Raymond Kimbrough, Richmond, Va.; Hans Krueger, New York; Emory Ladany, New York; Irving A. Lewe, Los Angeles; Earl Lafayette Loftis, Dallas, Texas; David Basil Morgan, Kansas City, Mo.; Edward Murphy, North Hollywood, Calif.; David J. Musman, Denver; Harry Nieman, Dayton, Ohio; Leo Orecklin, Detroit; Abraham Orfuss, New York; L. Stuart Planche, New Rochelle, N. Y.; Max Popper, Los Angeles; Charles O'Neal Rich, Salt Lake City; Harry Robinson Jr., Baltimore; Otto Ernest Lincoln Schmidt, San Francisco; Louis Schwartz, Bethesda, Md.; Oscar David Schwartz, Detroit; Abraham Albert Shapiro, Baltimore; Karl Steiner, Denver; Gordon Barclay Taylor, Hattiesburg, Miss.; Louis Henry Tobin, New York; Leonard Trilling, New York; Donald Hugh Williams, Vancouver, British Columbia, Canada; and Clyde Wood, Beverly Hills, Calif.

The following seven candidates were successful in the examinations and will be considered diplomates when they have completed five years in dermatology: Leo Marshall Columbus, San Francisco; Gage Helms, Long Beach, Calif.; Robert Wayne Helms, Long Beach, Calif.; Rodney F. Kendall, St. Paul; William Mulvihill, Beverly Hills, Calif.; Bernard F. Ryan, Los Angeles; and J. Walter Wilson, Los Angeles.



## Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

PYODERMIC MYIASIS IN CHILDREN LEON GOLDMAN, *Am J Dis Child* **69** 280 (May) 1945

In the American tropics, cutaneous myiasis is fairly common in children. It is usually of the pyodermic type with the formation of pustules, furuncles and carbuncles. These pyogenic processes represent varying degrees of secondary infection about the larval forms of the bot or warble fly, *Dermatobia hominis*. This short article is well illustrated.

NELSON PAUL ANDERSON, Los Angeles

SECONDARY SYPHILIS FOLLOWING PENICILLIN THERAPY OF GONORRHEA DONALD W. ATCHESON, *Am J Syph, Gonorr & Ven Dis* **29** 423 (July) 1945

The author reports the development of secondary syphilis in a patient who had received 100,000 units of penicillin for the treatment of gonorrhea twenty-five days previously. The course of events is of unusual value, as the patient was under complete control and observation, being confined to the Army air base, hence there was eliminated the possibility that syphilitic infection occurred after the penicillin was administered. The case report also demonstrates the inadequacy of treating syphilis with the same dosage of penicillin as that used for gonorrhea.

THE DIAGNOSIS OF GRANULOMA INGUINALE MADE BY EXAMINATION OF TISSUE STAINED WITH HEMATOXYLIN AND EOSIN S. H. POLAYES and LEONARD WILLIAMS, *Am J Syph, Gonorr & Ven Dis* **29** 425 (July) 1945

The authors corroborate the contention of Pund and Greenblatt that granuloma inguinale may be diagnosed by examination of biopsy material prepared by the usual routine—paraffin sections of tissue fixed in solution of formaldehyde which have been stained with hematoxylin and eosin. Two cases are cited by the authors illustrating the ease with which the "pathognomonic cell," with intracytoplasmic cysts containing the leishmania bodies, can be demonstrated in paraffin sections stained with ordinary hematoxylin and eosin.

THE RETARDATION AND SUPPRESSION OF EXPERIMENTAL EARLY SYPHILIS BY SMALL DOSES OF PENICILLIN COMPARABLE TO THOSE USED IN THE TREATMENT OF GONORRHEA H. J. MAGNUSON and H. EAGLE, *Am J Syph, Gonorr & Ven Dis* **29** 587 (Nov) 1945

The evolution of early syphilitic infection in rabbits was materially modified when small doses of penicillin comparable to those used in the treatment of gonorrhea in man were administered during the incubation period.

Four hundred units per kilogram injected intramuscularly five times at three hour intervals to a total of 2,000 units per kilogram, a dose which was less than one thirty-secondth of the amount, similarly administered, necessary to cure an established syphilitic infection in rabbits, either aborted the infection entirely or significantly prolonged the incubation period. Many of the delayed lesions were so small that comparable lesions in man might well have escaped detection, resulting in infections "asymptomatic" in effect if not in fact.

With penicillin being increasingly used as a primary therapeutic measure in gonorrhea, it is probable that the number of aborted, delayed or "asymptomatically"

acquired syphilitic infections will increase. Patients receiving treatment for gonorrhea should be kept under close serologic and clinical observation for a period of at least four months and preferably longer to guard against the latter two possibilities.

**STUDIES ON LIVER FUNCTION. LIVER FUNCTION IN EARLY SYPHILIS BEFORE AND DURING MASSIVE ARSENOTHERAPY.** M. M. HOFFMAN and F. KALZ, *Am J Syph, Gonorr & Ven Dis* **29** 596 (Nov) 1945

The functional status of the liver was evaluated prior to, during and after massive arsenotherapy in 22 patients with early syphilis by the following laboratory tests: the blood prothrombin concentration, the serum bilirubin level, the sulfobromophthalein sodium clearance and the rate of hippuric acid synthesis.

In only 3 patients were all these factors normal before therapy was started. During massive arsenotherapy the blood prothrombin concentration was decidedly reduced in 21 patients. In 10 patients at least one of the other observations indicated impairment of hepatic function. Function of the liver returned to normal within six months after cessation of arsenotherapy in all patients in this series.

Reduction of the prothrombin level did not occur in 10 patients who received 0.06 Gm of oxophenarsine hydrochloride (mapharsen) twice a week for ten weeks.

**TREATMENT OF GRANULOMA INGUINALE WITH ANTHIOMALINE.** LAWRENCE C. GOLDBERG, *Am J Syph, Gonorr & Ven Dis* **29** 608 (Nov) 1945

Sporadic reports on the use of anthiomaline (antimony lithium thiomalate), a pentavalent antimony compound, have appeared in the literature. The author reports a case in which extragenital granuloma inguinale was successfully treated with the drug.

**INGUINAL LYMPHOGRANULOMA VENEREUM IN THE MALE.** H. A. TUCKER, *Am J Syph, Gonorr & Ven Dis* **29** 619 (Nov) 1945

In the seven year period ending Sept. 1, 1944, 750 males were admitted to the Gorgas Hospital, Ancon, Canal Zone, with lymphogranuloma venereum. The incidence was about 6 per thousand male patients admitted to the hospital. Thirty-six and one tenth per cent were white persons from the United States. No significant racial reactions to the disease or its treatment were found. Primary penile lesions were noted in 13.3 per cent of the patients, 26.9 per cent of the patients had concomitant acute venereal disease. When the patients were seen early in the course of the disease, the best results followed sulfonamide therapy alone. Sulfathiazole came to be the drug of choice. Partial adenectomy was a definite adjunct of the treatment and was unhesitatingly used if the lymph nodes were fluctuant.

REUTER, Milwaukee

**LEISHMANIASIS.** ARDZROONY, PAKCHANYAN, J. A. M. A **129**:544 (Oct 20) 1945

Cultures of material taken from the ulcers of 2 soldiers who had recently returned from the Near East yielded *Leishmania tropica*. The diagnosis of cutaneous leishmaniasis usually is based on the clinical appearance of the lesion and on the presence of leishmania bodies in the stained preparations made from scrapings of the ulcer. This procedure is not conclusive, because occasionally yeastlike organisms or other extraneous substances from the lesion may be confused with leishmania bodies. If the ulcer occurs singly and is not extensive, local treatment with an ointment containing 2 per cent of antimony and potassium tartrate or local injections of 2 to 3 cc of a 1 per cent solution of berberine sulfate have therapeutic value. When the lesions are multiple, intravenous injections of step-up doses of pentavalent antimony preparations are necessary to produce curative results.

When a suitable culture medium is inoculated with material containing flagellar forms of *L. tropica* and incubated at room temperature for about ten days -

luxuriant growth of readily recognizable flagellates is obtained. The flagellates are leptomonad in form, are actively motile and colonize on the slanted portion of the blood agar tube.

CONGENITAL CATARACTS IN SISTERS WITH CONGENITAL ECTODERMAL DYSPLASIA  
H N COLE, HORACE K GIFFEN, J T SIMMONS and GEORGE M STROUD III,  
J A M A **129** 723 (Nov 10) 1945

Two sisters, aged 10 and 22 months respectively, had congenital cataracts, extreme internal strabismus, hypoplasia of the nails, almost complete alopecia, atrophic nasal mucosae and generalized hypoplasia of the skin. Typical major congenital ectodermal dysplasia of the anhidrotic type is considered to be a sex-linked recessive character (transmitted by the apparently normal female and affecting some of the males). However, cases have been recorded in which the ectodermal dysplasia has been classified as an incomplete dominant character (abnormality transmitted by direct descent from the diseased members of a family to some of their children, who in turn transmit it, and so on). The type of heredity in these 2 patients is considered to be of the incomplete dominant form.

COMPLETE SUBSIDENCE OF SCLERODERMA WITH DIHYDROTACHYSTEROL. EUGENE  
T BERNSTEIN and LEWIS A GOLDBERGER, J A M A **130** 570 (March 2)  
1946

A woman aged 70 underwent subtotal thyroidectomy for colloid goiter, and generalized scleroderma was observed one year after the operation. On the assumption that the scleroderma was caused by parathyroid deficiency resulting from the thyroidectomy, treatment with dihydrotachysterol was instituted. Complete regression and recession of all physical symptoms occurred with the exception of the maldistribution of pigment.

HENSCHEL Denver

ALLERGY TO CHEMICALS IN FLOUR. A CASE OF DERMATITIS DUE TO BENZOIC  
ACID. K A BAIRD, J Allergy **16** 195 (July) 1945

The author reports a case of recurrent dermatitis in a young baker, involving the face, neck, shoulders, arms and chest. Benzoyl peroxide when used for bleaching flour (improved flour) yields benzoic acid as a residue. This was considered the offending allergen.

The results of patch tests were as follows: with cake, bread and pastry flours containing "improvers," positive; with nonimproved flour, negative; with 6 per cent benzoic acid in liquid petrolatum, positive ("a definite papular rash in about six hours"); with liquid petrolatum, negative; with potassium bromate, negative.

The etiologic diagnosis was further substantiated by the fact that when the patient was entirely well a brief exposure to "improved" flour promptly resulted in a recurrence of the dermatitis.

MENDELSON, New York

NATURAL ANTIBODIES AGAINST YEAST-LIKE FUNGI AS MEASURED BY SLIDE-  
AGGLUTINATION. CHARLES H DRAKE, J Immunol **50** 185 (March) 1945

Agglutinins active in low dilutions against a variety of cellular antigens are common in blood serums. They are usually referred to as "normal" or "natural" antibodies, and several theories have been advanced to explain their presence without any known antigenic stimulation. Drake thought that some light might be thrown on their origin if serums were tested with suspensions of several different organisms, some of these would be common in the environment and others would be met only rarely by most persons. This investigation originated from the observation that the normal rabbit serum control frequently caused agglutination in a series of tests on the antigenic relations of several yeastlike fungi. These observations also afforded an opportunity of evaluating the usefulness of "slide

agglutination" with yeastlike fungi. "Tube agglutination" is not entirely satisfactory with cellular antigens in the size range of yeast cells.

Drake found that 81 per cent of the rabbit serums, reacted to at least one organism. *Saccharomyces cerevisiae* was most frequently agglutinated to the highest titer (42 per cent of the serums). The pattern of these findings supports the theory that a considerable number of so-called natural antibodies represent constituents of normal serum. This is indicated by the fact that the incidence of agglutinins appears to be independent of the likelihood of exposure to a given organism.

CORNBLEET, Chicago

SO-CALLED "PUSTULAR PSORIASIS" WILBERT SACHS and FRANCISCO SCANNONE, *J Invest Dermat* 6 349 (Dec) 1945

The authors in this presentation attempt to show that so-called pustular psoriasis is not a form of psoriasis.

They compare the pathologic features of several histologic sections of so-called pustular psoriasis with those of psoriasis and point out the difference present in the epidermis and the cutis.

It is also pointed out that these diseases differ in location, history, clinical picture and therapeutic response.

They therefore suggest that so-called pustular psoriasis may belong to the group of eczematous diseases.

PENICILLIN LOZENGES IN THE TREATMENT OF VINCENT'S STOMATITIS LUCIAN W STRONG JR and ERROLL W WILLETT, *U S Nav M Bull* 46 353 (March) 1946

The authors report that complete cures were obtained within a period of two to five days in over 400 cases in which Vincent's infection was treated with penicillin lozenges.

The lozenges which gave the best clinical results consisted of

Penicillin sodium	750 units
Acacia	30 Gm
Calcium stearate	5 Gm
Sucrose	65 cc

The method of treatment was first to spray the mouth with penicillin solution, 250 units per cubic centimeter and then to instruct the patient to dissolve a lozenge between the cheek and the gum every hour. A lozenge should also be chewed by the patient on retiring and at any time during the night that he awakens. Brushing of the teeth or the gums is contraindicated.

The lozenges retain their potency for four weeks when stored at room temperature.

PENICILLIN IN TREATMENT OF MADURA FOOT HOWARD E TWINING, HAROLD M DIXON and FRED D WEIDMAN, *U S Nav M Bull* 46 417 (March) 1946

Two cases are reported in which Madura foot, contracted outside the tropics, was treated with penicillin.

In the first case the disease contracted in Philadelphia, was produced by the species *Monosporium apiospermum* in a 57 year old Italian-born man and had progressed to the development of osteomyelitis. He received 3,700,000 units of penicillin over a period of twenty-seven days with an apparent cure at first. However the disease relapsed, necessitating an amputation.

In the second case, the disease, contracted in Alaska was caused by the species *Cephalosporium granulomatis* in a 40 year old Filipino sailor and involved only the soft tissues. He received 2,300,000 units of penicillin and at the end of eight months the cure appeared permanent.

Since Madura foot can be caused by a number of genera and species of fungi, a precise mycologic determination should be made before penicillin treatment is instituted in order that this therapy may be properly evaluated

RODIN, South Bend, Ind

THE TREATMENT OF SYCOSIS BARBAE BY PENICILLIN CREAM A BURROWS,  
B RUSSELL and H B MAY, *Brit J Dermat* **57** 97 (May-June) 1945

The authors investigated 21 cases of sycosis barbae bacteriologically and found that in 19 the eruption was caused by a strain of *Staphylococcus*, sensitive to penicillin. There were 13 cases in which the disease was of more than one year's duration, in 6 of these the eruption was cleared in an average time of six weeks, and in 6 there was improvement over an average period of six weeks. There were 6 cases in which the disease was of less than one year's duration, in 4 of these the eruption was cleared in an average time of two and a half weeks, and in 1 there was improvement over a period of five weeks. No improvement resulted from treatment in 2 cases, owing to the fact that the strains of bacteria were insensitive to penicillin.

The cream was prepared as follows. To 50 Gm of Lanette wax SX (an approximately 10 per cent sulfated or phosphated mixture of cetyl and stearyl alcohol) was added 250 cc of distilled water, and the whole was autoclaved under a pressure of 15 pounds (6.8 Kg) for twenty minutes. Fifty cubic centimeters of castor oil was sterilized by dry heat at 150 C for one hour. After sterilization of the oil, the two preparations were mixed and cooled to 60 C, and an appropriate amount of penicillin dissolved in water was added to make the final concentration 200 units per gram.

The patient was instructed carefully in a technic by which the cream could be aseptically removed from the jar. A knife or a spoon was sterilized in boiling water for three minutes and cooled under running tap water. The cream was then removed from the jar, spread on clean lint and applied thinly to affected areas two times a day.

THE RELATIONSHIP OF ACNE AND HYPERTRICHOSIS E LIPMAN COHEN, *Brit J Dermat* **57** 102 (May-June) 1945

The author examined 500 young women and could find no support for the statement that acne and hypertrichosis tend to occur together. BLUEFARB, Chicago

HAEMORRHAGIC TELANGIECTASIS D CAPPAN, *Brit M J* **1** 440 (March 31) 1945

The author reports a case of hemorrhagic telangiectasis in which there was a family history of four generations having the unusual features of polycythemia and headache following periods of anemia caused by epistaxis.

THE TOXICITY OF D D T G R CAMERON and F BURGESS, *Brit M J* **1** 865 (June 23) 1945

Experimental investigation of the toxicity of DDT (dichlorodiphenyltrichloroethane) revealed that DDT is tolerated in fairly large amounts when administered in single or repeated doses. The toxic levels are not easily reached when dilute solutions suitable for insect sprays are employed.

Human subjects whose clothing had been impregnated with DDT for prolonged periods had no ill effects.

DDT poisoning is characterized by nervous symptoms and severe damage of the liver. Usually changes in the blood picture precede the onset of the toxic stage.

## CONFLUENT SMALLPOX TREATED WITH PENICILLIN M A FOUIIS, Brit M J 1 910 (June 30) 1945

A patient with extremely severe smallpox was treated with a total of 800,000 units of penicillin

The lesions failed to increase in size after penicillin therapy was started, and most of them crusted without pustulation on or about the sixth day after the eruption appeared

Facial edema lasted no more than twenty-four hours

## SULPHONAMIDE RASHES AN ANALYSIS OF 500 CASES SEEN IN NORTH AFRICA AND ITALY G A GRANT PETERKIN, Brit M J 2 1 (July 7) 1945

From February 1943 to December 1944 over 650 cases of cutaneous sensitivity to sulfonamide compounds were seen by the authors. These reactions were due to drugs used in the treatment of many different diseases. The largest number of cases (72.2 per cent) were of the mild sensitization type, and an additional 17.2 per cent were of the contact dermatitis type. Most cases were due to sulfanilamide in powder form.

The safest drugs appeared to be sulfadiazine and sulfaguanidine. The color and the texture of the skin were apparently of no significance in the incidence of dermatitis.

It was noted that acriflavine and cocaine can reactivate a dermatitis due to a sulfonamide compound. The author warns against indiscriminate local application of sulfonamide compounds.

## TREATMENT OF EARLY SYPHILIS C HAMILTON WILKIE, Brit M J 2 900 (Dec 22) 1945

Wilkie, who is director of the venereal disease services at Leicester, England, registers a warning against the tendency to depend on penicillin alone in the treatment of acute early syphilis. He recommends penicillin plus at least one course of ten twice-weekly injections of an arsenical and a bismuth preparation.

## PENICILLIN DERMATITIS P D BEDFORD, Brit M J 1 51 (Jan 12) 1946

By means of patch tests the author proved the sensitivity of a patient to penicillin applied locally, which may have been induced by his having previously taken penicillin by mouth. He points out the risk of the haphazard use of penicillin-containing face powders and toilet applications envisaged in the popular press.

SHAW, Chattanooga, Tenn

# Society Transactions

## DETROIT DERMATOLOGICAL SOCIETY

Frank R. Menagh, M.D., *President*

Hermann Pinkus, M.D., *Recorder*

Jan 30, 1946

**Discoid and Disseminated Lupus Erythematosus** Presented by DR LOREN SHAFFER and Staff of the Department of Dermatology, City of Detroit Receiving Hospital

L. S., a Negro woman aged 27, presents typical lesions of discoid lupus erythematosus in a butterfly distribution on the nose, cheeks, eyebrows, and pinnae of both ears. She also has diffuse alopecia and dermatitis with considerable pigmentation of the scalp, posterior surface of the neck and upper part of the trunk. There is some punctate atrophy and follicular plugging on the scalp. In addition there are grouped follicular papules with a tendency to depigmentation on the back. The eruption began with a few small papules on the cheeks in June 1943. These gradually spread to the present involvement. The patient first became ill during the summer of 1944. She reported to the clinic at the City of Detroit Receiving Hospital in August 1944 with severe prostration, low grade fever and disseminated lesions at the sites of the present pigmentation. She was then sent to Eloise Hospital and Infirmary, where she remained until January 1945. Since then she has been hospitalized in the City of Detroit Receiving Hospital. She received antisyphilitic treatment from 1939 to 1942.

The Kahn and Kline reactions were positive. The red blood cell count was 3,050,000 and the white blood cell count 5,150, with 70 per cent neutrophils (45 per cent filamentous and 25 per cent nonfilamentous cells). Biopsy specimens were taken from the face in August 1944 and from the back in January 1945. Both showed changes typical of lupus erythematosus. The patient evidently received injections of olophenarsine hydrochloride and a bismuth preparation at Eloise Hospital and Infirmary.

### DISCUSSION

DR FRANZ L. BLUMENTHAL: I have seen this patient for some time at Eloise Hospital and Infirmary. Clinically, she showed all the characteristics of lupus erythematosus discoides of the face. On the body there was a grouped papular eruption looking much more like a lichenoid tuberculid than a syphilid. Since at that time, however, the Kahn reaction was strongly positive, antisyphilitic treatment was started. Today the patient's condition is much worse. The whole eruption is of much more acute character on the face as well as on the body, but the eruption on the body still looks mostly like some form of tuberculid.

DR A. C. CURTIS, Ann Arbor, Mich.: I was interested in seeing this case. It has seemed to me that the most extensive follicular plugging that one finds in lupus erythematosus is seen in Negroes. Why is this true? I believe that this Negro woman has disseminated lupus erythematosus of the subacute type.

DR FRANK R. MENAGH: Has this woman shown any elevation of temperature?

DR LOREN SHAFFER: She had a fever all the time she was at Eloise Hospital and Infirmary, however, the temperature was only 99 to 100 F. Since she has been here, her temperature has been normal. She shows pronounced prostration, which is characteristic of the general disseminated type. I think that it is unusual to see the combination that is seen in this case. In addition to the lupus erythema-

tosus, she has some lesions on the back in which I am interested, these are grouped follicular papular lesions with a tendency to leukoderma. Scattered disseminated lesions of lupus erythematosus with hyperpigmentation are also present on the back. I feel that these grouped papular lesions are probably atypical lichen scrofulosorum.

DR FRANZ L. BIUMENTHAL: We thought for some time that perhaps there was secondary syphilis, but, finally we came to the conclusion that we had to deal with some kind of tuberculid.

DR FRANK R. MENAGH: Would any one like to say anything about treatment?

DR ALBERT J. BOYLE (by invitation): I have read considerably in connection with this case and have noted the many features it has in common with cases of adrenal lesions. The patient has had persistent headache, fever, attacks of diarrhea, loss of weight, anemia, lesions of the mouth, low blood pressure, pigmentation and other symptoms and signs, all of which may be found in Addison's disease. She has menorrhagia, which might readily account for the anemia. Also she has syphilis. Occasionally syphilis is responsible for lesions of the adrenal cortex. It does seem, however, that lupus erythematosus disseminatus has many signs and symptoms compatible with disease of the adrenal cortex.

Recently it has been shown that the treatment of Addison's disease is assisted in some instances by the administration of testosterone. On this basis I should like to see this patient given testosterone. Incidentally, I believe that there has been reported a case of successful treatment of lupus erythematosus disseminatus by roentgen therapy to the ovaries, which leads one to speculate on the hormonal aspect.

DR FRANK R. MENAGH: In how many cases have changes been shown in the adrenal cortex?

DR ALBERT J. BOYLE (by invitation): I have never seen figures on this point. It is conceivable, however, that there are only selective functional changes of the cortex (production of ketosteroids), not structural changes of the whole cortex, and therefore there may be no demonstrable pathologic alterations.

DR A. C. CURTIS: In view of what has just been said, I should like to mention an article by Levine (Contratto, A. W., and Levine, S. A. Acute Lupus Erythematosus Disseminatus, *New England J. Med.* 221:602, 1939). His patient, like many other patients who have disseminated lupus erythematosus, was a young woman. Levine expressed the belief that an abnormality of the production of ketosteroids might have something to do with the causation. So the patient was sterilized. She died of pneumonia three months after the sterilization but had no active lesions at the time of death.

I have sterilized 2 patients with acute lupus erythematosus by radium. One woman was severely ill and had been studied for five years because of an unknown fever before the typical lesions of disseminated lupus erythematosus finally developed. Her sterilization occurred five years ago, and she is well today.

In a recent article in the *Annals of Internal Medicine* by Rose and Pillsbury (Rose, E., and Pillsbury, D. M. Lupus Erythematosus [Erythematoses] and Ovarian Function: Observations on a Possible Relationship, with Report of Six Cases, *Ann. Int. Med.* 21:1022, 1944), the cases of 5 patients who were sterilized are reported. Their results also are suggestive of improvement in some cases. Because in so many cases acute disseminated lupus erythematosus occurs in young women, I believe that sterilization is justified in some instances.

**A Case for Diagnosis (Leukemid, Contact Dermatitis?)** Presented by DR LOREN SHAFFER and Staff of the Department of Dermatology, City of Detroit Receiving Hospital.

N. C., a white woman aged 71, presents rather sharply defined acute erythematous dermatitis of the 'V' of the neck and upper part of the chest. Similar lesions are present in the cubital fossae and on the intimal aspect of the left knee.



The patient has had chronic stasis dermatitis and ulceration of the left ankle for many years. In March 1944, an acute dermatitis developed on the left leg. This was considered simple stasis dermatitis, and ligation of the saphenous vein was performed in July. The dermatitis, however, did not improve but spread to the neck and arms in September. Leukemia was first diagnosed in July 1944. At that time she had 39,000 white blood cells, including 94 per cent lymphocytes. She received 600 r of filtered roentgen rays to four areas of the anterior surface of the trunk in September 1944, after which the pruritus and dermatitis disappeared completely. The white cell count of the blood dropped to 10,500 with 69 per cent lymphocytes. The white cells have been increasing gradually, the last count was 17,300 on November 27.

The present condition suggests dermatitis venenata, however, the patient feels that it is similar to that of the previous attack, which responded well to high voltage roentgen ray therapy. The case is presented as an instance of a possible toxic manifestation of leukemia. No biopsy was performed. Results of other laboratory examinations were noncontributory.

#### DISCUSSION

DR JAMES R. ROGIN: I am willing to accept the diagnosis of leukemic pruritus, but I do not see how one can call it leukemid.

DR CLYDE HASLEY: I think that these lesions are due to stasis dermatitis, inasmuch as they appeared mainly on the ankles and legs, and I am inclined to think that is an important factor. The leukemia is probably a secondary consideration, but inasmuch as the blood count was greatly reduced with radiation one certainly has to take into consideration this contributing factor. It is hard to reconcile these lesions with a diagnosis of leukemid.

DR HERSCHEL ZACKHEIM (by invitation): Previous treatment had not relieved the itching of the legs, but after roentgen therapy the itching subsided. Later, however, the itching began to reappear, and the blood count showed a rise.

DR FRANK R. MENAGH: It is notable that in some cases of lymphoblastoma, particularly the Hodgkin type, one does not get too good a result, so far as the pruritus is concerned, immediately following therapy with roentgen rays. This patient volunteered the information that she painted the lesions on her ankles with a balsam salve.

DR LOREN SHAFFER: Nobody has mentioned the erythema and dermatitis around the neck of this woman. It is suggestive of a contact dermatitis. The question is: Is this a contact type of dermatitis, or is it a manifestation of leukemia? She had a similar dermatitis before, which was not relieved by any local application until she had high voltage roentgen ray therapy. Then it disappeared and subsequently reappeared with an increase in the blood count. I questioned the diagnosis of leukemid, and I agree that the typical leukemid is a papular eruption. It does not necessarily contain the infiltration of the skin, however, I suspect because of the varied distribution of the lesions on the neck that it was actually a contact dermatitis.

#### A Case for Diagnosis (Superficial Epitheliomatosis?) Presented by DR JAMES R. ROGIN

A. E., a white man aged 45, first noticed spots on the middle of his chest and in the sternal region, as well as over his spine, about fifteen years ago. These lesions have been slowly progressive in size and in number during the past fifteen years but have at no time produced any symptoms, and he would not be conscious of them at all, except for being able to see those on his chest. He has enjoyed good health, and there is nothing significant in his general medical history. Serologic tests for syphilis have elicited negative reactions previously and do so at present.

The patient presents over the midsternal region and scattered on the chest maculopapular discrete lesions, varying in size from that of a split pea to that of a half-dollar. For the most part these lesions begin discretely, but in some places they become confluent. They vary in color from a light fawn to a deep brown, almost black. They are covered with a scale, but when the patient was first seen a few weeks ago, before treatment, most of the lesions were covered with rather tightly adherent thick crusts. Similar lesions are present over the spine, from the cervical to the lumbar region.

Crusting has disappeared for the most part after the use of a mild ammoniated mercury and salicylic acid ointment. Most of the lesions show a definite smooth white atrophy, and some of the newer lesions, for example, the one on the left side of the chest from which the biopsy specimen was taken, showed atrophy with diffuse reddish telangiectasia on the surface. This telangiectasia is not perceptible in the older pigmented lesions. The most striking feature of the lesions at present is the combination of pigmentation, atrophy and telangiectasia.

Histologic sections were presented.

#### DISCUSSION

DR HOWARD PARKHURST, Toledo, Ohio. This is one of the few cases of this disease that I have seen in which the patient did not have psoriasis. I do not know whether this man gives any history of having received arsenic at any time. I was interested to note that the lesions were limited strictly to the area from the waistline up and that he stated that he had gone with his trunk exposed to the sunlight for a number of summers several years ago, prior to the development of this eruption. Whether or not the light may have been a factor is of great interest, it seems to me.

DR A C CURTIS, Ann Arbor, Mich. I thought that this eruption was rather typical of intraepithelial epithelioma, possibly Bowen's disease. The pigmentation and the distribution were unusual. By tangential light a threadlike rim was seen about some of the lesions. I agree with the diagnosis of superficial epitheliomatosis.

DR HERMANN PINKUS, Monroe, Mich. (demonstrating the microscopic section on the screen). Most of the surface of the section unfortunately is denuded of epithelium. This is probably the result of medication. Thus one cannot say to what extent and in which form epitheliomatous changes were present. Only one end of the section is covered with epidermis, and there is a small cluster of cells of basal type within or just below the epidermis. This spot permits one to make a diagnosis of superficial epithelioma of basal cell type.

DR A C CURTIS, Ann Arbor, Mich. Well, the pathologic section is not characteristic of Bowen's disease, but it is characteristic of an intraepithelial epithelioma of the basal cell type.

DR FRANZ L BLUMENTHAL. I could not find much moisture in the lesions, which I assume to be characteristic of Bowen's disease.

DR JAMES R ROGIN. Before this man had any medication, which consisted of an ointment of ammoniated mercury and salicylic acid, the lesions were crusted, hence I thought for a time the eruption might be Darier's disease. But after a week of medication, the patient came back with the crusts all gone and the lesions as one now sees them. He has had no medication now for the past ten days.

**A Case for Diagnosis (Lupus Pernio, Sarcoid?)** Presented by DR LOREN SHAFFER and Staff of the Department of Dermatology, City of Detroit Receiving Hospital.

F S, a white woman aged 48, presents a confluent infiltrated granulomatous lesion involving the cheeks and nose. A similar lesion is present on the outer aspect of the left arm and is approximately 5 cm in diameter. The lesions are elevated and bluish red and have a smooth surface. No searing or apple-jelly nodules are demonstrated.

The disease began sixteen years ago with a bluish red nodule on the right cheek. This gradually increased to the present size and has been stationary for several years. The lesion on the left arm began several years ago. The patient has been under observation for some years at Harper Hospital. She first reported to our clinic in June 1944. She received twelve low voltage roentgen ray treatments of 70 r, unfiltered, at weekly intervals to September 20. The lesions improved decidedly with this treatment, and the patient was able to get a job. She returned on Jan. 12, 1945 with the present recurrence.

A roentgenogram of the chest on January 12 showed that the patient had had parenchymal tuberculosis. Nodular exaggeration of the root zones raised a question of Boeck's sarcoid or possibly lymphoblastoma. A microscopic section obtained from Harper Hospital revealed epithelioid cell tubercles in the deeper parts of the corium. This is characteristic of the lupus pernio variety of sarcoid.

#### DISCUSSION

DR GEORGE VAN RHEE: I saw this patient at Harper Hospital. The clinical diagnosis at that time was sarcoid, and microscopic examination confirmed this.

DR JOHN H. COBANE: The pathologic sections are typical of sarcoid and not of lupus vulgaris. There are some nodules in her lung, and I feel from the roentgenograms of her lung that the diagnosis is sarcoid.

DR LOREN SHAFFER: I might say that I presented this case, and it was my impression, which is evidently wrong, that the patient had been under care at Harper Hospital with the diagnosis of lupus tumidus, however, the biopsy establishes, I think, beyond question the diagnosis of sarcoid. It would be interesting to get a roentgenogram of the phalanges. She had eight injections of oxophenarsine hydrochloride without improvement. Incidentally, sarcoid will occasionally respond to the arsphenamines.

**Lymphoblastoma** Presented by DR LOREN SHAFFER and Staff of the Department of Dermatology, City of Detroit Receiving Hospital

H. W., a Negro aged 55, has an enormous tumor, measuring approximately 14 by 16 cm., which is granulomatous and elevated approximately 4 cm. and presents areas of ulceration. The tumor is firm. The cutaneous surface, where not ulcerated, is smooth and shiny and moderately fixed. The mass extends from the fifth rib to the umbilicus. There is moderate bilateral axillary adenopathy. The patient appears otherwise in good health and has relatively little discomfort.

Approximately fifteen months ago the patient noted a small subcutaneous nodule on the abdomen near the xiphoid process. This increased slowly in size for three months and then rapidly for the past year. He has had no pruritus and says that he has had no cutaneous lesion at this site. The Kahn reaction of the blood was negative on Jan. 21, 1945. The hemoglobin was 8.5 Gm. and the white blood cells 6,700, of which 90 per cent were neutrophils. Another blood count, on January 25, showed 7,500 leukocytes, with 82 per cent neutrophils (71 per cent filamentous and 11 per cent nonfilamentous), 10 per cent lymphocytes, 6 per cent monocytes and 2 per cent eosinophils. A roentgenogram of the chest was reported as showing no specific evidence of metastatic malignant growths in the chest, ribs or dorsal portion of the spine. Three histologic sections are presented: (A) abdominal mass, (B) axillary nodes, and (C) skin of the abdomen near the tumor.

**Pathologic Report** (Dr. Bert E. Stofer): Microscopic examination of the abdominal mass (A) shows a nonencapsulated tumor composed of fairly densely packed cells which vary considerably in size and shape. The majority exhibit a fairly dense nucleus and scant eosinophilic cytoplasm which tends to become fibrillar in some areas. Mitotic figures are seen. Microscopic examination of the axillary tissue (B) shows hyalinized tissue infiltrated with cells identical to those found in the tumor mass. No nodal tissue is recognized. Tumor cells are seen invading the nerve sheaths. Microscopic examination of the skin (C) shows a ribbon of cells in the upper part of the corium, extending in some areas into the

papillae and into the subcutaneous tissue and the panniculus adiposus. It is in this section that the tumor cells show their greatest variability. Mitoses are frequent, and giant cells with up to four nuclei are relatively common. The chromatin in some areas is rather dense and in other areas decidedly granular. The accessory organs of the skin are surrounded by masses of tumor cells. The final diagnosis was lymphoblastoma. The exact type cannot be determined from these slides alone. The tumor itself suggests reticulum cell sarcoma. The cutaneous sections are more suggestive of mycosis fungoides or leukemia cutis. Imprint preparations, studies of bone marrow and repeated blood counts are suggested.

## DISCUSSION

DR R. C. JAMIESON: I have nothing to say. I do not think that this case belongs to a dermatologist.

DR LOREN SHAFFER: An unusual feature of this case is the general condition of the patient. His physical condition is surprisingly good. Roentgenograms of the chest revealed no abnormalities. I made the suggestion on the record that the tumor would probably be radiosensitive. It began as a nodule and has rapidly mushroomed, especially during the past year. The pathologic picture would suggest mycosis fungoides.

DR A. C. CURTIS, Ann Arbor, Mich.: Some time ago we saw an infant who had vulvar lesions suggestive of the changes seen in these sections. We have followed her for five months. The lesions cleared rapidly with roentgenotherapy. The last roentgenogram showed a punched-out area in the pelvis due to metastasis. This patient has a cellular response of the reticulum type, and the tumor is a lymphoblastoma.

**Blastomycosis.** Presented by DR LOREN SHAFFER and Staff of Department of Dermatology, City of Detroit Receiving Hospital.

T. C., a Negro aged 45, presents a sharply defined granulomatous lesion with elevated slightly verrucous borders which involves the axillary surface of the left arm, extending from the axilla to the middle of the arm. Partial healing has occurred in the central areas. The borders of the lesion have arciform configuration, and some superficial ulceration is present in the borders.

The lesion began two years ago as a small papule which slowly increased in size. The patient consulted various physicians and received local therapy and at one time six injections of an arsenical. Repeated serologic tests have elicited negative reactions. He reported to Dr. Franz Blumenthal in August 1944 and received roentgenotherapy and potassium iodide by mouth. He improved with this treatment but discontinued it, and the disease relapsed. Roentgenograms revealed no extension of blastomycosis in the chest and left shoulder girdle. Kahn and Kline reactions of the blood were negative, other examinations were not significant.

Histologic sections show chronic granulomatous inflammation with abscesses and atypical proliferation of the epidermis. Numerous blastomycetes are present in giant cells and free in the tissue. Sulfonamide compounds have been used locally and internally for the last several weeks. Improvement is questionable.

## DISCUSSION

DR FRANZ L. BLUMENTHAL: I saw the patient last summer and found organisms in the pus. Orally he got 1 Gm. of potassium iodide three times a day and twice weekly intravenously 10 cc. of a 10 per cent solution of sodium iodide, combined with 100 r. of roentgen rays filtered through 2 mm. of aluminum weekly for five weeks. With this treatment he improved greatly, but then he left the city. Today he is in much better shape than he was when I saw him the last time. At the time I saw him first he showed all the clinical characteristics of blastomycosis.

**Lichen Ruber Moniliformis Kaposi** Presented by DR HERMANN PINKUS  
for DR FELIX PINKUS, Monroe, Mich

M M, a white woman aged 19, was previously presented at Grace Hospital in October 1937, at Harper Hospital (American Academy of Dermatology and Syphilology) in January 1938 (*ARCH DERMAT & SYPH* 38 317 [Aug] 1938) and at Henry Ford Hospital in January 1942. Previous suggested diagnoses were pyogenic infection with keloid formation, due to trauma, psoriasis, lichen planus, pyodermatitis, artefacts, keloid and larva migrans. The patient supposedly had smallpox at the age of 8 months and infantile paralysis at the age of 21 months. She wore a brace for several months which caused irritation and recurrent blisters on the legs and ankles up to the age of 4 years (a younger brother has epidermolysis bullosa). She had scarlet fever in January 1935. This was followed by a generalized vesicular (?) eruption which was treated with ammoniated mercury. The patient was in University Hospital, Ann Arbor, Mich, in May 1936, at which time a biopsy was made. The lesions cleared, except those on the legs, which have persisted ever since. Various forms of treatment, including occlusive dressings, brought temporary improvement. Additional biopsies were performed at Grace Hospital (1937) and at Henry Ford Hospital (1942).

Examination on Oct 21, 1944 showed the patient to be well developed and well nourished. Cutaneous lesions were confined to the legs and, to a minor degree, the thighs. The legs showed a bizarre picture of bluish red firm elevated cords forming an irregular network on the anterior and lateral sides of the legs and dorsa of the feet. Some lesions were present on the calves and on the thighs. The cords were up to 1 cm wide and almost as high, and their surface was partly shiny, partly covered with a thin silvery scale and partly crusty. They exhibited deep transverse furrows at irregular intervals, and numerous white milium-like bodies were visible below the surface. Within the meshes of the network and in the surroundings there were numerous brownish red flat or slightly umbilicated papules. The patient said that the lesions itched and hurt, and she admitted that she scratched a good deal and had the habit of digging the milia out with a needle.

Five superficial roentgen ray treatments of 72 r were given at weekly intervals to each of five fields on the anterior and lateral surfaces of the legs. The thighs were shielded from the rays. Arsenic in increasing doses was taken by mouth from October 1944 to Jan 6, 1945. No topical treatment was advised. The patient was admonished not to scratch or otherwise injure the skin. After four roentgen ray treatments (Nov 18, 1944) the lesions were much flatter and began to get more silvery scales. The milia had almost disappeared. Subjective symptoms were much improved. On Jan 6, 1945 there was some edema of the legs, and the lesions were more painful and succulent, with several vesicles and bullae up to the size of a pea on the crests of the cords. This reaction was considered as due to arsenic, and vitamin B complex capsules were substituted. At present, the lesions show continuing improvement and are much flatter throughout, and some have disappeared leaving atrophic scars. Milia have become more numerous again.

**Histologic Examination** Section of a "keloid" band from the right shin (Oct 12, 1944) was reported on as follows. The epidermis is atrophic and hyperkeratotic. Several cystic dilated sweat ducts filled with horny matter and resembling milia are found in the upper part of the corium. The corium has the structure of a vascularized scar in which the elastic fibers are absent. There are scattered lymphocytic infiltration and some small clusters of mast cells. Section of a small flat papule from the left thigh (Nov 11, 1944) revealed that there are acanthosis and hyperkeratosis, with increased mitotic activity and formation of epithelial giant cells in the epidermis at the periphery of the lesion. The central part shows separation at the dermoepidermal junction and hyalinization of the basal membrane or of the entire papillary body, with the epidermis undercutting the hyalinized portion. There is slight subepidermal cellular infiltration around numerous capillaries. Many melanophores are present.

## DISCUSSION

DR HARTHER L KEIM This is the fourth clinic at which this girl has been presented. She was seen at Henry Ford Hospital on one occasion, and she was shown at Grace Hospital, too. I was interested in the histologic sections. Of course, I have not the time to go into a discussion of whether or not lichen ruber moniliformis is a variety of lichen planus, but I shall refer briefly to the work of Wise and Rein (ARCH DERMAT & SYPH 34 830 [Nov] 1936). They were convinced that it was an entirely different thing and based their opinion largely on the histologic picture. In their article they showed these areas of necrosis of the epithelium, which they stated are rather characteristic, and pointed out the absence of any characteristic lichen planus infiltrates below the epithelium. In the section which was taken in 1942 it is interesting to note that there is shown one of these typical necrotic lesions, but to my mind the cellular infiltrate in the corium is compatible with the diagnosis of lichen planus. So perhaps this is a good example of a transitional case. In 1938 the consensus was lichen planus.

DR ARTHUR E SCHILLER At the time the patient was seen at Grace Hospital, the picture was different. The raised portions were verrucous and covered with much more scale. I think that the diagnosis then was lichen planus.

DR FELIX PINKUS (by invitation), Monroe, Mich. In my opinion the cutaneous eruption of this woman is the same disease one finds in the atlas of Kaposi (also *Vierteljahresschrift für Dermatologie und Syphilis* 18 571, 1886) called by him lichen ruber moniliformis. There is a bundle of red brown stripes, equally elevated and equally wide, radiating down the anterior surface of the legs from a narrow center on both knees. Some of the stripes end free at the sides of the calves and on the backs of the feet and on the ankles. Most of them cross one another at acute angles, forming lozenges. Much of the free space of these rhombi is filled with one or more small papules of the same color as the stripes. These papules are similar to those of the case of Kaposi, although there are some features which are similar to lichen planus. There are many clinical and histologic important differences in all the biopsies my son has made. On the other hand, the structure in this case does not resemble the histologic picture of the best American case, that of Dr Wise and Dr Rein (ARCH DERMAT & SYPH 34 830 [Nov] 1936). There is another point which distinguishes this case from a case of real lichen planus, that is its beginning. Many years ago, the disease started as a bullous eruption diagnosed as epidermolysis bullosa, and now there is the most interesting fact that in the younger brother of this patient, at the same age as it happened to his sister, blisters developed following trauma that cannot be diagnosed otherwise than as epidermolysis bullosa. So far we were inclined to accept the suggestion of Wise and Rein to separate lichen moniliformis from the typical lichen planus, to leave the diagnosis undecided and to substitute the designation of Wise and Rein, "morbus moniliformis." Today we got some slides of an older biopsy specimen, made by Dr Menagh, and in them the picture is rather different. There is heavy infiltration and certain changes in the epidermis, similar to the description of Kaposi. So we have to start once more, returning to the old case of Kaposi by which the question began in 1886.

DR FRANK R MENAGH I think that this might be the case that connects the two groups.

DR A C CURTIS, Ann Arbor, Mich. The patient was seen by Dr Davis in Ann Arbor in 1935, and the eruption was alleged to have appeared after scarlet fever eighteen months before. That would date the beginning as 1933. When the patient was seen in 1936, the question was whether the eruption was an atypical lichen planus or a pyoderma. Dr C W Weller did not think that the patient was characteristic of lichen planus. I have wondered since seeing the patient whether this was not a keloidal response in a person who has had an infectious process in lesions of lichen planus.

DR FRANK R MENAGH I think that all agree that this case takes a great deal of "steam" out of Wise and Rein's paper.

DR HERMANN PINKUS, Monroe, Mich (demonstrating microscopic slides on the screen) Through the courtesy of Dr Curtis, we have the section taken at Ann Arbor, Mich, in 1936. The main feature of this specimen is the cysts lined with cornifying stratified squamous epithelium and apparently formed by the sweat ducts just beneath the epidermis. The corium is fairly vascular, but there is hardly any cellular infiltration. The epidermis is thin and partly torn off. The histologic picture is similar to that of the most recent biopsies.

The specimen removed at Henry Ford Hospital, a section of which Dr Menagh lent me, shows a different picture. In it one sees similar cornified cysts in the upper part of the corium, but, in addition, one sees a dense cellular infiltration consisting of lymphocytes and leukocytes in a vascular stroma. The epidermis is partly necrotic and partly covered with a thick scaly crust. Close to the edge of the lesion there is much atypical proliferation of the epidermis. It is quite possible that a great deal of this inflammatory reaction is unspecific and due to trauma and secondary infection. I doubt that the epidermal necrosis of this section may be compared with the peculiar necroses described by Wise and Rein. These authors performed ten biopsies on their patient and were surprised at the small amount of inflammatory infiltration they found. My father and I were similarly surprised when we performed biopsies in our case, and the first one at Ann Arbor, Mich, also shows this lack of cellular infiltration. It has been suggested that this lesion represents a keloidal change following either lichen planus or trauma. I think that the great vascularity speaks somewhat against keloid, and it must be remembered that the second biopsy specimen taken by me is from a small early papule.

#### **Epidermolysis Bullosa with Formation of Scars and Milia** Presented by DR HERMANN PINKUS

D M, a boy of 9 years, is the brother of M M, the woman with lichen ruber moniliformis. He also was presented to this society at Henry Ford Hospital. For several years blisters have been developing over pressure points, particularly on the feet, knees and elbows. Some of these blisters leave scars in which white kernels accumulate. The patient presents a tense thick-walled bulla just proximal to the nail of the right third toe. There are several atrophic scars on the shins, knees and elbows. At the knee and elbows there are also red slightly raised firm plaques, the largest 2 by 1 cm, in which are embedded firm whitish bodies of pinhead size which resemble milia.

#### **DISCUSSION**

DR LOREN SHAFFER I think that this case is extremely interesting, and the papular infiltrated lesions are suggestive of the same process (lichen ruber moniliformis) as noted on the woman presented. Unfortunately, there has been no biopsy. Another interesting thing to me would be the suggestion that this disease may be familial. As far as I am concerned, I think that probably the child has two different diseases, the epidermolysis bullosa, which is not active, and these new lesions, which are papular infiltrations.

#### **NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILOLOGY**

Harry C Saunders, M D, *Chairman*

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Feb 6, 1945

#### **Circinate Sarcoid (Boeck's)** Presented by DR ABRAHAM WALZER

A H, a clerk selling fruit, is presented from the dermatologic clinic of the Jewish Hospital of Brooklyn. There is no history of tuberculosis or diabetes in

the patient or in his family. He had a penile chancre for which he was treated by intramuscular and intravenous injections. The Wassermann reaction of his blood was strongly positive. After being treated for a number of months he was told that the Wassermann reaction had become negative, and treatment was discontinued. About six years later, or seventeen years ago, he married, and at that time the Wassermann reaction of his blood was said to be negative. His wife subsequently gave birth to three children, their ages at present being 15, 14 and 11 years. The Wassermann reactions of their blood, as well as that of his wife's blood, have always been negative.

About two years ago he noted "red spots" on his legs, which gradually increased in size and extent. The lesions on the face appeared about six months later. They did not itch. About six months after the onset of the rash he was seen by his physician who, in the course of a general examination, found that the Wassermann reaction of his blood was strongly positive. He has since been treated for syphilis at a local clinic.

At present the patient shows the following lesions: 1. There are large rings on the right leg and thigh, varying from 1 to 5 or 6 inches (2 to 12 or 15 cm) in diameter. The border is about  $\frac{1}{4}$  inch (0.6 cm) in width, raised, hard, nodular, of a violaceous color and sharply demarcated. The skin within the ring is faintly pink and soft and gives a suggestion of atrophy. In one of the larger-ringed lesions of the leg, the central part is brown and feels somewhat indurated. 2. The left leg and thigh also show similar annular lesions which have joined and formed large serpiginous patches with similar raised red indurated borders, enclosing a brown indurated area within which are coin-sized patches of apparently normal skin. 3. The cheeks, the forehead and the temporal areas show flat raised erythematous plaques the size of a dollar or larger. They are smooth, indurated and not sharply outlined. Some show superficial telangiectatic vessels.

A complete physical examination, including neurologic and ophthalmologic ones, revealed nothing abnormal. Roentgenograms of the chest showed perihilar adenopathy. Roentgenograms of the hand showed a normal structure. The results of the hematologic studies, including those for total lipids, cholesterol and phospholipids, as well as blood sugar, were within normal limits. A urinalysis showed nothing abnormal. The Wassermann reaction of the blood was positive, but the Wassermann reaction of the spinal fluid was negative. An intracutaneous test with tuberculin in a dilution of 1:10,000 elicited a negative reaction.

A histologic examination of two sections, one removed from the face and the other from the leg, showed the following changes:

**Lesion of the Face.** Throughout the upper part of the cutis there were numerous epithelioid cells arranged in small masses (tubercles), with little or no surrounding cellular reaction. There was considerable interstitial edema in the subepidermal region, with scattered giant cells. The overlying epidermis showed no important change.

**Lesion of the Leg.** Throughout the entire cutis there were numerous tubercles composed of epithelioid cells and giant cells, with no central necrosis. In the upper part of the cutis the vessels were dilated and the walls thickened. There was a mild diffuse small round cell and wandering connective tissue cell exudate. The overlying epidermis was irregularly acanthotic.

#### DISCUSSION

DR. EUGENE TRAUGOTT BERNSTEIN: This is a classic case of the annular type of sarcoid. The histologic picture showing naked epithelioid tubercles pathognomonic of this entity confirms the clinical diagnosis.

DR. LOUIS CHARGIN: Obviously the eruption is not syphilis. Whether one is dealing with sarcoid or necrobiosis, it is not easy to tell. The eruption closely resembles that of a patient presented by Dr. Silver last month, in diagnosing it most discussers agreed on necrobiosis. The histologic picture of sarcoid is not at all rare in necrobiosis. Perhaps a point against this diagnosis is the sex of the



patient, the lipid disturbances being more frequently observed in women. Moreover, the lesion on the face would fit in better with sarcoid.

DR ABRAHAM WALZER. When a lesion is shown by histologic examination to be definitely sarcoid, it must be accepted as such. However, when the histologic designation is "sarcoid-like," it does not necessarily imply sarcoid. There are sarcoid-like structures associated with tuberculosis, leprosy and other diseases, as well as with some reactions to injected foreign bodies. These lesions are no more true sarcoid than a lichenoid structure is true lichen planus. In the patient presented the lesions on the face are unquestionably sarcoid, both clinically and histologically, while those on the legs may be questioned clinically. With a definite histologic report of sarcoid, those lesions too can be nothing but sarcoid.

DR LOUIS CHARGIN. The histologic slides in the case presented last month were declared by Dr Sachs to be those of sarcoid, not a sarcoid-like lesion, yet most of the discussers favored necrobiosis as the most likely diagnosis.

DR EUGENE TRAUGOTT BERNSTEIN. In necrobiosis lipoidica diabetorum fat droplets are able to penetrate through damaged walls of the blood vessels by diapedesis into the cutis. These extracellular fat droplets, stained with sudan III, are imbibed into the tissues, causing necrosis. The disease has nothing to do with diabetes. In some instances it is a sequel of hypercholesteremia or some other variety of hyperlipoidemia. In necrobiosis lipoidica diabetorum one does not find Masson's cells (epithelioid nevus cells of Merkel-Ranvier).

DR ABRAHAM WALZER. With regard to the case presented last month, the histologic examination, I understand, has definitely shown the lesion to be sarcoid and not sarcoid-like. The disease must therefore be accepted as sarcoid and not necrobiosis.

#### Chronic Lymphangitis Presented by DR ABRAHAM WALZER

B F, a widow aged 47, is presented from the dermatologic clinic of the Jewish Hospital of Brooklyn. She gave a history of having had scarlet fever with renal and aural involvement at the age of 8 years, meningitis at 12 and a number of attacks of pneumonia. Her right ear was still discharging, and she was completely deaf on that side. About sixteen years ago she had "toxemia of pregnancy," and her blood pressure at that time was over 300 systolic. About four or five years ago she had a "tumor" removed from the roof of the mouth.

The present infection began about seven or eight months ago. The central part of the face and the right upper eyelid suddenly became red and swollen, accompanied with a slight rise in temperature (99.5 to 101.5 F). This lasted for a few days and then gradually subsided. These attacks would recur every week or two, but the recession was never complete.

On Aug 11, 1943, the patient was admitted to the hospital and after a thorough investigation was discharged in two and a half weeks with a diagnosis of chronic glomerulonephritis. There was no improvement in the lesion of the face.

At present the nose, the cheeks and the chin are swollen, indurated, faintly red and somewhat tender. The erythema is not sharply outlined. The upper eyelid is swollen but is soft and erythematous.

The patient also has a mild stomatitis with leukoplakia-like spots. The roof of the mouth shows a mild abrasion at the site where the "tumor" was removed. She has no teeth and wears upper and lower dentures. She also presents lesions of perleche at both labial commissures.

#### DISCUSSION

DR LOUIS CHARGIN. This seems to me to be a case of so-called habitual erysipelas, a recurrent form of this disease often associated with lymphangitis. There is evidently a focus of infection in the nose or the mouth, and something acts to start a new attack every so often. I think that this would be an excellent case for a thorough trial of penicillin therapy. If the infection is not controlled, a solid edema of the face is likely to develop.

DR DAVID BLOOM I agree with Dr Chargin When solid edema has developed, no medication is of any benefit In this case there is a chance to prevent solid edema

DR EUGENE TRAUGOTT BERNSTEIN I believe penicillin should be given to a total of about 1,000,000 units, in a dosage of 25,000 units every three hours

DR ABRAHAM WALZER It has been suggested that this is a case of erysipelas The absence of the crimson-red color, a smooth shiny glazed surface and a high temperature, all speak against erysipelas However, the recurring attacks of solid edematous swelling, which never recedes completely but is progressive and permanent, speaks more for a recurring lymphangitis or a solid edema of the face

#### Urticaria Due to Cold Presented by DR ABRAHAM WALZER

T F, a married woman aged 44, is presented from the dermatologic clinic of the Jewish Hospital of Brooklyn There is no history of atopy The patient had an appendectomy twenty-five years ago and "neurasthenia" ten years later for four years About two and a half years ago she had a number of attacks of "Meniere's disease"

The present ailment began suddenly about ten years ago The patient noted that on exposure to cold in the winter her face and her hands swelled and became red and itchy This persisted for about fifteen to thirty minutes after exposure Cold drinks or ordinary bathing in cold water did not affect her, but bathing in the sea would induce dizziness and fainting spells

Complete physical and hematologic examinations and a urinalysis revealed nothing abnormal The Wassermann reaction of the blood and also that of the spinal fluid were negative

When an ice cube is placed on the skin of the forearm for two or three minutes, the skin becomes red and in about another minute a pronounced wheal forms, assuming the shape of the cube of ice

#### DISCUSSION

DR CHARLES WOLF There is no doubt that this is a rather classic case of physical allergy, and one does not frequently see such a straightforward cause and effect phenomenon Since Dr Walzer attacks dermatologic diseases from the allergic standpoint, it would be interesting to have him tell the members how he expects to secure a therapeutic effect in this patient

DR LOUIS CHARGIN If this patient is not much disturbed by the disease, I think it best to institute no treatment However, if necessary, an attempt should be made to desensitize her to cold Such desensitization has been reported in the literature Histamine phosphate in these cases is without effect It does not matter in what manner it is employed

DR EUGENE TRAUGOTT BERNSTEIN I agree with Dr Chargin that in physical allergy, particularly to cold, desensitization by gradual adaptation to cold plays an important part It is known that exposure to cold produces swelling of the lips and the tongue, lacrimation, coughing and so forth Cold anaphylaxis may cause death while one is bathing, as was pointed out by Horton The subject elicited much attention in the literature (Horton, B T *Proc Staff Meet, Mayo Clin* 2 276, 1927) A sudden onset of urticaria due to cold makes bathers so helpless that they can hardly be rescued from drowning The loss of consciousness is the sequel of cerebral edema resulting from the same mechanism as does the temporary loss of vision

DR ABRAHAM WALZER The term "physical allergy" has been employed to describe these types of cases—a hypersensitiveness to a physical force, such as cold, heat and sunlight The term, however, is not a good one because allergy denotes a reaction between chemicals Nevertheless, the constant and frequent use of this term justifies its employment for hypersensitiveness to such physical forces

With regard to treatment for urticaria due to cold, nothing has as yet been found to be a cure in these cases. In line with the procedure by which patients are desensitized to proteins by frequent and progressive administration of minute quantities of the offending antigen, it has been suggested that a similar course be followed in respect to allergy to cold. Bathing in cold water the temperature of which is gradually and progressively reduced has been tried but with no success. The sensitivity to physical forces apparently simulates the sensitivity to drugs in which desensitization cannot be accomplished by administering the drug in minute doses over a long period. Histamine phosphate has been injected in these cases, on the theory that histamine is released at the site of the wheal induced by cold and is the direct cause of the reaction. The injected drug is therefore supposed to desensitize the patient to histamine, but in practice this does not occur.

It is a purely theoretic supposition that in urticaria due to cold the cold releases "allergens" and that antibodies to these allergens are formed which can be passively transferred. While reports of experiments demonstrating this do appear in the literature, the majority of attempts to repeat these experiments have failed. In the division of allergy of the Jewish Hospital in Brooklyn, passive transfer of immunity to heat or cold has not been successful in a single instance, after many attempts over a long period.

DR EUGENE TRAUGOTT BERNSTEIN. Nineteen cases have been reported in which it was possible to demonstrate the presence of an antigen-antibody reaction by means of passive transfer tests. Among those reporting are E. Lehner (*Zentralbl f Haut- u Geschlechtskr* 41 199, 1932), E. Liebner (*Zentralbl f Haut- u Geschlechtskr* 34 406, 1930), F. Bernstein (*Dermat Ztschr* 64 242, 1932), J. Affolter (*Schweiz med Wchnschr* 63 841, 1933), E. C. E. Bodenstein (*Zentralbl f Haut- u Geschlechtskr* 52 364, 1936) and other investigators.

#### Dermatitis Medicamentosa (Fixed Eruption Due to Arsenic) Presented by DR ABRAHAM WALZER

A. H., a Negro woman aged 55, presented from the dermatologic clinic of the Jewish Hospital of Brooklyn, complains of an eruption on the body and in the mouth.

There was no history of syphilitic infection. About four years ago, during the course of a general examination, a positive Wassermann reaction of the blood was found, and the patient has since been treated at a local clinic with an arsenical and a bismuth compound. About fifteen months ago, after she had received approximately thirty injections of a bismuth compound and twenty injections of neoarsphenamine, it was noted that after an intravenous injection of neoarsphenamine "sores" developed in the mouth and raised red edematous pruritic lesions on the body. These would subside in three or four days and leave pigmented spots, only to recur at the same sites after every subsequent injection of the arsenical. This drug was discontinued about one year ago.

The patient shows scattered dark blue or black pigmented round or oval patches varying in size from that of a dime to that of a dollar or larger. They are sharply outlined and not elevated. Most of the lesions are on the upper part of the body.

A urinalysis, blood counts and a complete physical examination revealed no abnormality. The Wassermann reaction of the blood was 4 plus.

#### DISCUSSION

DR LOUIS CHARGIN. I think that one is dealing with a fixed eruption due to the arsphenamines. This patient will probably be found sensitive to all arsphenamines, less so, perhaps to oxophenarsine hydrochloride than to the others. Fortunately this patient shows no lesions on the face, and treatment with the arsphenamines should be avoided if possible to obviate such an occurrence. It would be of interest to determine whether she is likewise sensitive to antipyrine and phenolphthalein—in other words, whether she shows polyvalent sensitivity.

DR OSCAR L LEVIN Fixed eruptions from arsphenamine were formerly common. These are not observed so frequently nowadays, and I have not observed any in private practice in the past few years. About twenty years ago there was a patient at the Cornell Clinic who would show an exacerbation of a fixed eruption after each injection, and after seven or eight the use of arsphenamine was stopped and silver arsphenamine was given instead, without the production of an eruption. I agree with Dr Chargin that it is not advisable to endanger a patient by the continued use of arsenicals when a patient who is not in the infectious stage presents a fixed eruption.

DR ABRAHAM WALZER The question of polyvalent sensitization in patients with a drug sensitivity is an interesting one, and it is not rare. However, one must bear in mind the fact that not infrequently the rash due to a specific drug may be reproduced nonspecifically by the ingestion of another drug and also by physical and mental states during the interval immediately following the recession of the drug rash. However, after the rash has been gone for some time, these nonspecific factors will not produce it again.

#### **Urticaria Pigmentosa** Presented by DR JESSE A. TOLMACH

S. B., a man aged 52, born in Poland, employed as a dress operator, has had a cutaneous eruption for the past four or five years. This began on his abdomen and spread rapidly to other parts of his body. There is only slight itching at times. No one in the patient's family has had a cutaneous eruption as far back as he can remember. He has been suffering for a number of years from disease of the gallbladder. A cholecystectomy was performed in 1941. A right inguinal hernia developed several years ago.

The skin of the trunk, the shoulders, the arms, the buttocks and the thighs presents a generalized eruption consisting of multicolored macules, ranging from brownish to yellowish to slate-colored stains. On friction by hand or from tight clothing, the lesions turn into papules which may assume the size of large welts. The lesions predominate on the trunk and the shoulders, are vast in number and are arranged according to cleavage.

The urine was normal, and the Wassermann reaction of the blood was negative. The blood count showed 4,000,000 erythrocytes and 9,600 leukocytes, with 47 per cent neutrophils, 21 per cent monocytes, 30 per cent lymphocytes and 2 per cent eosinophils.

Biopsy performed by Dr Sachs showed with the hematoxylin and eosin stain that the vessels of the middle and upper parts of cutis were dilated and there was a sparse, small, round and wandering connective tissue cell infiltration. Considerable edema was present throughout the cutis. The overlying epidermis showed no important change. There was a pronounced increase in the number of mast cells. The microscopic diagnosis was urticaria pigmentosa.

#### DISCUSSION

DR JOEL SCHWEIG (by invitation) The question of the causal relationship between chronic disease of the gallbladder, hepatic damage and urticaria pigmentosa is interesting and deserves further investigation. Whenever the patient experiences pressure and tightness due to clothing, corresponding swelling and itching result.

DR OSCAR L. LEVIN I agree with Dr Schweig that there may be a relationship between disease of the gallbladder and the liver and urticaria pigmentosa. I have frequently observed such a relationship between disease of the gallbladder and the liver and urticaria, angioneurotic edema and allied diseases. The reactions may be due to a decrease in the detoxifying action of the liver or possibly to the presence of an infection or a toxin in the gallbladder. In every case of urticaria or urticaria pigmentosa an investigation into the history of disease of the gallbladder should be made. I have also observed excellent results in urticaria following lavage of the gallbladder.

DR DAVID BLOOM As in young children, so in adults urticaria pigmentosa must be considered a nevus eruption. The presence of disease of the gallbladder may be considered as coincidental.

DR OSCAR L. LEVIN In the young, one should also bear in mind the possible association of an eruption with a disorder of fat metabolism and the possible relationship to disease of the liver.

DR CHARLES WOLF It is commendable to project theories on cause and effect in disease, but it would be difficult to prove that there is a relationship in this case in view of the fact that disease of the gallbladder is a common affliction. In the course of a year several thousand patients are operated on in the city of New York for disease of the gallbladder and associated diseases of the liver. The members, as dermatologists, know that urticaria pigmentosa, both the juvenile and the acquired form, is a rare disease, the cases seen in the lifetime of any dermatologist are few. One cannot accept flimsy theories as an explanation of a disease as mysterious as urticaria pigmentosa. It is a mast cell formation having to do with the reticuloendothelial system. Many hemopoietic organs may be involved in the causation of the disease.

DR ABRAHAM WALZER I think that urticaria pigmentosa is being confused with chronic urticaria. There is no fundamental connection between the two. Urticaria pigmentosa is not urticaria, and the term is therefore a misnomer. The only resemblance, and it is a slight one, is the dermatographia present in urticaria pigmentosa. Otherwise, both clinically and histologically, they are decidedly different entities. Urticaria pigmentosa is not an allergic manifestation and has no relation to food or any other antigen. As far as is known, it has no relation to disease of the liver or the gallbladder or to any focus of infection. In the infantile form it resembles a nevus more than anything else.

DR JOEL SCHWEIG (by invitation) It is true that urticaria pigmentosa is not an urticaria in the true sense of the term, or an urticaria with pigmentation, it is a definite, separate entity capable of producing welts as seen in ordinary urticaria. Although the etiologic factor of urticaria pigmentosa is unknown, observations have been made in cases of urticaria pigmentosa that the manifestations were associated with hepatic damage. Our case reveals this relationship distinctly, as the urticaria pigmentosa appeared shortly after the first symptoms of the disease of the gallbladder became manifest. Of course, it might be coincidental. The argument that one does not frequently observe urticaria pigmentosa in association with disease of the gallbladder and that there is therefore no connection between the two is not valid, as one rarely sees diabetes associated with necrobiosis lipoidica, for instance, and yet nobody will deny the interrelation of the two diseases.

Roentgen ray therapy is being advocated for urticaria pigmentosa, but the benefit is limited. The eruption is known to have cleared spontaneously.

#### **Dermatitis Lichenoides Chronica Atrophicans (Csillag)** Presented by DR OSCAR L. LEVIN

E. F., a married woman aged 50 and a native of Puerto Rico, whose occupation is that of housewife, entered the Mount Sinai Hospital clinic one week ago complaining of an eruption of eighteen months' duration. She stated that white spots first appeared on the skin of the chest and spread to the shoulders.

On the right side of the chest are seen discrete small whitish polygonal flat atrophic papules. On the left side there are similar lesions and also others which show a tendency to become confluent and form patches. The centers of many of these show patent empty follicular orifices. There are also follicular scaly plugs. On the back are similar lesions, which show more prominence of the follicular plugs and which on palpation impart a nutmeg grater sensation. On the mucous membrane of the left labium majus there is a white flat pigmented plaque showing several small depressions, probably the result of papules similar to those observed elsewhere.

Biopsy specimens were taken from lesions on the chest, but as yet there has been no report

## DISCUSSION

DR DAVID BLOOM The appearance of the eruption is that of lichen sclerosus et atrophicus of Hallopeau The characteristic follicular plugs are present in younger lesions and atrophy without plugs in older lesions

Harry C Saunders, M D, *Chairman*

Frank Vero, M D, *Secretary*

March 6, 1945

**Dermatitis Medicamentosa (Iodide)** Presented by DR EUGENE F KELLY

T C, an Italian-born man aged 46, is presented from Vanderbilt Clinic with an eruption of the face, the neck, the trunk and the extremities of six years' duration A squamous cell epithelioma of the lip is undergoing treatment

In 1917, while the patient was in the Italian army, a penile lesion developed, and there was a positive Wassermann reaction of the blood He received intramuscular injections of mild mercurous chloride and later a preparation of bismuth for a period of one year After a four year interval treatment was resumed sporadically, consisting of a preparation of bismuth given intramuscularly Seven years ago, in this country, intravenous treatment was begun and received at irregular intervals for a year Six years ago a series of intravenous injections was given and also iodides in capsule form Shortly after this medication was started abscesses and boils began to appear on the body, the face and the extremities He took in all about 100 capsules over a period of three months He stopped taking them when dizziness and heartburn appeared and the abscesses increased in number

On the face, the neck, the trunk and the extremities there are numerous irregular, oval and round pigmented and depigmented scars distributed bilaterally There are some active lesions on the trunk and on the cheeks consisting of follicular papules and small furuncles There is a large scar on the back of the neck, the result of a carbuncle

The urine was normal except for the presence of albumin (1 plus) The Wassermann and Kline reactions of the blood were negative

## DISCUSSION

DR A BENSON CANNON We thought that the case was of particular interest because of the large, irregular, deep scars, apparently with great loss of tissue, which I do not recall having seen before in dermatitis due to an iodide I think that Dr Kelley has demonstrated that they are due to iodides in that the man is appreciably better since treatment with the drug was discontinued

DR GEORGE C ANDREWS I was particularly interested in this man because of the epithelioma on the lower lip He has been exposed to much sunlight He has had a biopsy and irradiation, which accounts for the crusted appearance

**Behçet's Syndrome, Abortive Form (?) (Recurrent Aphthous Oral Lesions and Recurrent Genital Ulcerations)** Presented by DR HELEN O CURTH

E O C, a single woman aged 23, is presented from Vanderbilt Clinic complaining of lesions of the mouth and vulva which have occurred since childhood The patient was born in New York city of Irish and French Canadian parentage, and has been under observation since 1942 She is next to the youngest of nine brothers and sisters Three children died in early childhood No other member of the family has a similar disease

The patient has suffered from recurrent lesions in the mouth since childhood. Menstruation began at the age of 14. One year earlier she noticed the first vulvar lesions, and these have returned often since. At the beginning they appeared between menstruations, but lately they sometimes coincide with menstruation. Some attacks begin with chills. Temperatures around 101 F may persist for a few days. The ulcerations heal with deep scars and destruction of the vulva. At the beginning of the attack a mucous discharge is discernible, and sometimes the inguinal nodes on the involved side are inflamed. In former years attacks were accompanied by severe pains in the left or the right calf. Lately the attacks of oral ulcerations have been so severe and frequent that the patient has not been free from them at all. The patient denies sexual relations. She has always been in good general health. She has never been absent from New York city for any length of time.

Physical examination reveals no significant abnormality. There is no enlargement of the lymph nodes. The eyes are normal. The tonsils are small and can hardly be considered foci of infection. Examination of the teeth in November 1944 showed the upper right central incisor and the lower right cuspid to be abscessed, but these have since been removed. The lips, the tonsils, the tongue, the soft and the hard palate, and rarely the buccal mucosa, are the sites of superficial or deeper tender erosions which are covered with an exudate and surrounded by a red halo. The ulcerations show a deep, dirty base. Scars of healed ulcerations are seen on the tongue, the lower lip and the soft palate.

The vulva is the site of an extensive, indurated, atrophic and destructive process. Both labia majora show extensive scarring. The posterior part of both labia majora was removed in a plastic operation (1942), and a biopsy was made of the tissue. Both labia minora are enlarged and show multiple fenestration. When an ulceration is present, it shows in the early stage a large, necrotic area surrounded by a hemorrhagic border. Later a deep ulceration is seen which may measure 2 cm in diameter. The base of the ulcer is granulating, and the border is infiltrated.

The uterus is slightly retroverted, and the small adnexa are not felt. The cervix was found on one occasion to be clear, and at another to show an erosion.

The laboratory examinations revealed no albumin or glucose in the urine. Repeated Wassermann and Kline tests elicited negative reactions. The number of white blood cells ranged between 11,850 and 15,900, with hemoglobin 92 per cent and red blood cells 4,850,000. Polymorphonuclear leukocytes were 72 per cent, small lymphocytes 22 per cent, large lymphocytes 5 per cent, and mononuclear cells 1 per cent. The sedimentation rate was 35 to 40 mm per hour. Blood cultures during the patient's stay in the hospital showed no growth, nor did nose and throat cultures. The results of blood agglutination tests for *Eberthella typhosa* O and H and for *Salmonella paratyphi* A, B and C were negative. Results of Frei and Ducrey tests were repeatedly negative. Old tuberculin tests in a dilution of 1:10,000 elicited negative reactions.

Bacteriologic examinations of the genital lesions, including dark field examinations, scrapings for Donovan bodies and smears for chancroid bacilli and inclusion bodies, were negative. Slides and cultures for fungi were negative, as were repeated inoculation tests. Smears for gonococci from the cervix and an ulceration were negative. *Bacillus crassus* was once seen in great numbers in a smear from the genital lesion, but was not seen in the biopsy specimen. In a culture hemolytic *Staphylococcus aureus* and *Staphylococcus albus*, but no anaerobes, were found.

No inclusion bodies or *Bacillus crassus* were seen in smears from the oral lesions. *Staphylococcus aureus*, *Staphylococcus albus* and streptococci were found on culture.

Suspensions in saline solution were made from genital and oral scrapings. The suspensions were inoculated into mice, guinea pigs, cotton rats, embryonated hen's eggs and chick embryo tissue cultures of the L<sub>1</sub> and Rivers type. There has been no evidence of the growth of any viral agent.

The course and treatment were as follows. In May 1942 a plastic operation of the vulva was performed in the Sloane Hospital for Women. For a while afterward the patient had no recurrence of the genital lesions. Later the lesions began to recur fairly often. She was successively treated with 3 per cent sulfathiazole ointment, potassium permanganate soaks, and estrone cream locally to the genitals, and with hydrogen peroxide, analgesic tablets and estrone cream locally in the mouth.

General treatment consisted of injections of liver extract, nicotinic acid 100 mg twice daily, sulfathiazole internally (2 Gm daily for six days) and penicillin 1,710,000 units (given at the Presbyterian Hospital) and removal of two abscessed teeth. The patient has avoided brushing her teeth for several weeks, and has eliminated chicken, eggs and oatmeal from her diet.

All of these therapeutic attempts were given up when the impression was gained that the condition got worse rather than better. While the patient was receiving penicillin, especially, the extent of the oral lesions was larger than ever.

Biopsy of a genital ulcer showed granulation tissue at the base of the ulceration. The tissue was swollen and edematous. Areas below the ulcer were the site of a chronic inflammatory reaction with aggregation of polymorphonuclear leukocytes, lymphocytes and plasma cells. The infiltration was not found in any significant distribution around the blood vessels, which appeared thickened. Giemsa stains did not reveal the presence of any organisms. The diagnosis was genital ulceration of unknown cause.

#### DISCUSSION

DR A. BENSON CANNON. I think that Dr. Curth deserves great credit for having called our attention to these cases. She has worked extremely hard on them, and has made a real contribution to the society and to dermatology.

DR FRED WISE. Dr. Curth deserves great credit for calling our attention to cases of this syndrome. I believe that this is the second case she has presented. Many diseases are characterized by lesions involving the vulva and the mouth, sometimes coincidentally and sometimes separately, and, aside from *Bacillus crassus*, bacteriologic findings have for the most part been negative. Many observers believe that a virus is the causative agent. It will require much more investigation to reveal the cause of these ulcerations. I hope that Dr. Curth will be successful in this field of investigation and will tell us more about the causation.

DR GEORGE C. ANDREWS. One feature is the chronicity, as these cases run on for so many years. The classification is difficult, because it is hard to know where *ulcus acutum vulvae* ends and Behçet's syndrome begins, as many cases of *ulcus acutum vulvae* have been accompanied by oral lesions. The question is whether those cases of both oral and genital lesions were formes frustes of Behçet's syndrome. I happened to see in my office today a young woman with ulcerations similar to those presented by this patient. About five years ago she had extensive ulcerations in the vulva, sulfanilamide helped her so that she did eventually get entirely well, but she came in today with sores on her vulva again. She has had the condition for many years. We had a case of Behçet's syndrome at Presbyterian Hospital a while ago which was reported in the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY* after presentation before the New York Dermatological Society. The patient had the disease for about ten years, with sores on the penis, iritis, conjunctivitis and blepharitis. He had subungual abscesses which were different from ordinary ones in that they would disappear after a few weeks by themselves. He also had ulcers in the mouth. The disease began with hydrops of the right knee joint, which is one of the common symptoms of Behçet's syndrome.

DR MABEL G. SILVERBERG. I should like to suggest the use of smallpox vaccination. I had a case of chronic ulcers of the tonsil and buccal mucosa, the patient was vaccinated, a violent reaction occurred, and the lesions cleared up in forty-eight hours and have not recurred.



DR HELEN O CURTH The question of *Bacillus crassus* is a perplexing one. This case does not differ from Lipschutz' original description of *ulcus vulvae acutum*. One of his cases was also accompanied by oral lesions, which he thought was coincidental. Since then, most observers have found *B. crassus* in genital lesions but have been unable to find it in the oral lesions. Matras, however, found *B. crassus* in the oral lesions. He, Samek and Fischer also obtained positive blood cultures. It seems to be the opinion of other observers that *B. crassus* would be found in the genital tract of many women, whether they have these ulcerations or not. The fact that men have the same kind of genital and oral lesions would also speak against the etiologic role of *B. crassus*. I called this case an abortive form of Behçet's syndrome because I was impressed by the similarity of the oral and genital lesions with those seen in cases of the fully developed syndrome. It may take twenty years before ocular lesions develop. I am thankful for the suggestion of smallpox vaccine and will try it. With regard to ocular lesions, one should insist on a picture of iritis, iridocyclitis or uveitis with hypopyon. I consider that the form of ocular lesion seen in this syndrome

#### Moniliasis Presented by DR JAMES LOWRY MILLER

R V, a girl aged 7, is presented from Vanderbilt Clinic with an eruption of the scalp, the mouth and the finger nails of two and one-half years' duration. The patient was admitted in August 1942, complaining of red, crusted lesions involving the face and the scalp which had been present for two months. Examination at that time showed the entire scalp to be covered with a heavy crust, with many bald areas interspersed with clumps of hair. Perleche lesions were present at the corners of the mouth, and red, pea-sized papular areas covered with crusts were present on the chin and the forehead and around the nose. Both thumb nails were dystrophic.

On the scalp there are many red, bald areas between which are areas of normal scalp. A number of the red areas are covered with thick, adherent crusts. No scarring is seen. On the forehead there are a few pea-sized, red, crusted papules. The corners of the mouth are red and covered by a white, lacy pellicle which extends back on the mucous membrane of the mouth. The left first and third and the right index finger nails are dystrophic with chronic paronychia at their bases.

General physical examination revealed no abnormality except that the child is pale and somewhat underweight. Cultures from the scalp, the finger nails, the mouth and the feces were all positive for *Monilia albicans*. The complete blood count was normal.

Treatment has consisted of undecylenic acid, sodium propionate, methylrosaniline chloride, salicylic acid, injections of crude liver, and many other remedies. Methylrosaniline chloride (gentian violet) has been the most efficacious remedy, and one nail and accompanying paronychia have cleared under treatment with fuming nitric acid.

#### Moniliasis Presented by DR JAMES LOWRY MILLER

E R, a white man aged 25, was admitted to the Vanderbilt Clinic on August 8, 1944, suffering with a generalized dermatitis which has been present since he was 3 months old. It began in infancy on the buttocks and gradually spread to involve most of the body. It was treated as an infantile eczema, and at the age of 5 all lesions completely disappeared, and he remained clear for one year. Since that time cutaneous lesions similar to the presenting eruption have existed at all times. He has never had any intestinal or respiratory symptoms. During the last year he has noticed loss of hair from the scalp and the eyebrows. The toe nails have been involved for years, and the finger nails more recently have shown changes.

Large infiltrated erythematous scaly patches varying from pea size to palm size are scattered over the entire body, including the hands and the face. On

the scalp there are a number of similar patches. The hair on the entire head is thin, but no atrophic areas are present. The finger nails are dystrophic, particularly at the sides. There is no paronychia. Perleche lesions are present at the corners of the mouth. On the mucous membranes at the side of the mouth and on the tongue there are white, lacy pellicles.

Cultures were positive for *Monilia albicans* from the feces, the sputum and the tongue. Repeated cultures from the nails, the scalp and the skin have been negative.

The Wassermann reaction of the blood was negative.

Sections of the cutaneous lesion disclosed acanthosis, hyperkeratosis and parakeratosis. Epithelial cells with eosinophilic cytoplasm were present. A chronic inflammatory reaction within the derma was seen. The diagnosis was chronic dermatitis.

A roentgenogram of the chest in the posteroanterior projection showed no evidence of recent parenchymal infiltration. Both costophrenic angles are clear. The tracheal air column appeared in the midline. The heart was not abnormal. Some calcium depositis were seen in both hilar regions.

#### DISCUSSION

DR GEORGE M LEWIS. I agree with the diagnosis. The clinical features are typical, and there is a positive culture. The question of therapy is one of the most difficult in dermatology, and the outlook as to the future must be reserved. Fortunately, these cases are rare.

DR BEATRICE M KESTEN. The habitus of patients with moniliasis is characteristic. This seems to make it impossible to combat the infection in either the skin or the intestinal tract. Even giving methylosaniline chloride in capsules has not been effective.

DR WILLIAM CURTH. The man has a brother with the same infection. Both have been seen here in years gone by, and reported by others (Satenstein, D. *Moniliasis*, *ARCH DERMAT & SYPH* **28** 124 [July] 1933, Lapowski, B. *Miliary Pustular and Erythematous, Squamous, Nummular Dermo-Epidermite in Progressing Centrifugal Plaques* (Gougerot), *ARCH DERMAT & SYPH* **30** 144 [July] 1934, **30** 308 [Aug] 1934).

#### A Case for Diagnosis (Moeller's Glossitis? Glossitis Due to Vitamin B Deficiency? Glossitis Due to Phenobarbital? Presented by DR WILLIAM CURTH

F. C., a Rumanian woman aged 62, is presented from Vanderbilt Clinic with an eruption in the oral cavity of five months' duration. In October 1944 small blisters which ruptured after a few days appeared on the tongue and left the tongue sore. Her physician considered pemphigus and referred her to the Vanderbilt Clinic. Sodium perborate and sodium bicarbonate were applied without success. For about thirty years there have been occasional "canker sores" which have become more frequent since the teeth were removed twelve years ago and the patient began to wear dentures. She cleans them with Squibb's tooth paste. Her general health has been fairly good with the exception of some increase in the blood pressure, for which she has taken phenobarbital since September 1944. The menopause occurred at the age of 47.

The sides of the anterior half of the dorsum of the tongue show irregular, sharply defined red areas, neither elevated nor depressed, with a greatly thinned surface and an absence of papillae. The central portion of the tongue presents whitish papillae. The posterior papillae are not enlarged. Vesicular or bullous lesions were not seen during a period of observation of three weeks, in spite of continued phenobarbital medication.

Examination of the blood showed hemoglobin 102 per cent, red blood cells 5,150,000, white blood cells 8,700, polymorphonuclear leukocytes 59 per cent and lymphocytes 41 per cent. Examination of stomach contents after an Ewald test

meal showed total hydrochloric acid 84 degrees and free hydrochloric acid 80 degrees Wassermann and Kline reactions of the blood were negative Microscopic examination and culture for fungi were negative

A biopsy specimen from the upper edentulous gum showed a pronounced hyperemia with an inflammatory exudate and edema in the corium The epithelium of the basal cell layer was destroyed in many places, with desquamation at the sites of the destroyed epithelium The diagnosis was desquamative gingivitis

Daily applications of an estrone ointment resulted in considerable improvement of the condition of the gums and the tongue She also received three injections of a liver extract, 6 units each, on February 14, 23 and 28

#### DISCUSSION

DR ISADORE ROSEN I should be inclined to a diagnosis of drug eruption rather than Moeller's glossitis Pain and the other features usually associated with Moeller's glossitis are entirely absent The fact that the patient has been taking large doses of phenobarbital over long periods would tend to corroborate the diagnosis of drug eruption

DR CHARLES WOLF If this is a manifestation of avitaminosis, I should like to know why estrone was applied to the gums

DR FRED WISE In Jadassohn's "Handbuch," Moeller's glossitis is described as a symptom of pernicious anemia In this patient no signs of pernicious anemia are present The possibility of a drug reaction must be entertained in lesions of this kind, despite a negative personal history

DR A BENSON CANNON When this patient was first seen at Vanderbilt Clinic, several of us thought of syphilis and of phenobarbital Dr Rosen presented a case which was the exact counterpart of a syphilitic tongue, which it was thought to be until proved due to phenobarbital I am pleased to hear tonight for the first time that the woman has been taking phenobarbital, and with Dr Rosen's case in mind, I would not hesitate to attribute the condition of the tongue in this case to the use of that drug

DR WILLIAM CURTH This woman has been given injections of liver extract and has improved considerably Our dental department performed a biopsy of the gum and suggested treatment with an ointment containing estrone, which was given her The patient still suffers from hot flushes

#### Urticaria Due to Cold (Improved with Histamine Injections) Presented by DR J GARDNER HOPKINS and DR BEATRICE M KESTEN

D G, a white woman aged 55, a Russian housewife, came to Vanderbilt Clinic on Feb 13, 1940, complaining of itching and swelling of exposed areas when subjected to cold, dating from December 1939 While out in the cold the patient's face began to itch and felt numb When she came indoors her face was swollen Since then each time the patient goes out in the cold her face and extremities itch, and red blotches appear and then swell After she comes into the warmth the symptoms subside in an hour or so When cold water or ice touch the skin or even when the patient eats ice cream the mouth itches and burns, and the lips swell There have been no hives from other causes

The general health is good except for frequent headaches, often associated with being in the cold, hoarseness for the past year and arthritis

Submerging the hands in water 20 C or lower, or applying an ice cube to the skin for one minute produced redness, swelling and wheals which itched Injection of histaminase or epinephrine previous to application of ice afforded no protection from hives when subjected to cold Local contact with ice after iontophoresis with histaminase gave partial protection

Intradermal tests with mecholyl and carbaminoylcholine were negative Passive transfer tests for cold agglutinins were also negative

The patient was given 15 to 60 units of histaminase a day orally for six weeks with no relief From May 1940 to May 1944, except during the summer months,

the patient received an injection of histamine phosphate weekly or bimonthly. The initial dose was 0.001 mg intracutaneously, and this was slowly increased to 0.4 mg. From October 1944 to date the patient has received an injection of histamine azoprotein weekly. The initial dose was 0.05 cc given subcutaneously.

Since November 1944 the patient has had no hives. When the temperature reaches 10 C to 15 C her face tingles and feels tight, but there is no perceptible swelling. If the patient eats ice cream the tongue and lips prickle.

#### DISCUSSION

DR MAURICE J COSTELLO I presented a case before the Manhattan Dermatologic Society about two months ago, in which the patient showed a similar picture. Every time she was exposed to cold air she experienced swelling of the cheeks, the eyelids, the hands and the ankles. The intradermal administration of small doses of histamine phosphate completely cured the disease in two months. If histamine is to be of use at all, it should be indicated in the physical allergies.

DR GEORGE C ANDREWS Dr Bernstein's ideas on passive transfer are not fully accepted—by Robert Cooke, for instance, who recently wrote an article in the *Journal of Allergy* stating that those examples of passive transfer in cold and heat allergies have not been fully substantiated, and he doubts that there are antibodies that can be passed on in these physical allergies.

DR BEATRICE M KESTEN It is possible to accustom patients to cold by baths, by graded histamine injections, and by giving histamine orally—that is, by putting it on the mucous membranes of the mouth. It would seem that injection of a haptene (histamine plus globulin) is effective.

#### Ainhum Presented by DR FRANK VERO

A S, a Negro aged 60, is presented from Vanderbilt Clinic with a lesion of the right small toe of two years' duration.

The patient was born in Florida and lived in the Philippines from 1908 to 1911.

For the past two years the patient's right small toe has gradually become "pinched off" by a constricting band at the base. The process was completely painless until recently, when he began occasionally to have a "burning sensation" in and around the toe.

Examination shows the base of the right small toe to be constricted by a sclerotic ring. There is considerable maceration between the toes.

Microscopic examination of the toe nails was positive for fungus.

#### Calcification of Gluteal Regions Following Injections of Heavy Metals (Mercury) Presented by DR F PHILIP LOWENFISH

L F, a man aged 57, is presented from Vanderbilt Clinic with an affection of the buttocks which has been present for fourteen years. The patient has been under observation for treatment of syphilis since October 1928. Prior to this he had one hundred and fifty intramuscular injections of a preparation of mercury and one hundred intravenous injections of arsphenamine in the old Vanderbilt Clinic, three years before this date. In 1931 a pronounced induration of metal-like quality was noted over both buttocks. No lumps or nodules were felt. In 1928 the induration about the buttocks was unchanged, and the patient did not complain of any discomfort or pain. In January 1944 he began to suffer intense pain in the buttocks, and the area seemed much harder with lumplike and nodular masses, and it had become more extensive. Because of continuous pain the patient was referred to the surgical department for opinion and biopsy. A nodule was removed from the left buttock in February. He was treated in the physical therapy department with diathermy and static wave treatments to both buttocks. After six months this treatment was discontinued, there was little improvement. In January 1945 the pain was getting more intense, and

the patient complained of hardness and difficulty in sitting down, with the pain and induration extending up into the lumbar region. Because of osteoarthritis he was referred to the arthritis clinic a few days ago, where they felt that he was not a problem for them but suggested the fracture clinic for this type of pain referable to the low part of the back.

In 1931 a roentgenologic examination of the pelvis showed numerous streaky shadows of metallic density scattered throughout the region of the buttocks. The bones of the pelvis did not suggest abnormality.

In 1938 an anteroposterior roentgenogram of the pelvis showed an increase in the number of streaky shadows present in the region of the buttocks bilaterally since the examination of July 23, 1931. Otherwise there had been no significant change.

In 1944 a roentgenologic examination of the pelvis showed the presence of numerous streaky shadows of calcium density in both buttocks, indicative of previous administration of heavy metal. The bony structures of the pelvis appeared normal.

In January 1945 a roentgenologic examination of the pelvis and the spine showed no evidence of bone abnormality. The previously noted shadows of metallic density resulting from intramuscular heavy metal therapy were about the same in distribution and appearance. Osteoarthritis was seen in the lumbar spine.

In February anteroposterior and lateral views of the pelvis showed the previously described shadows of metallic density to be more numerous in this examination. In the anteroposterior roentgenogram they extended from the anterior superior part of the spine to the lesser trochanter. The bones of the pelvis did not suggest any abnormality.

The Wassermann and Kline reactions of the blood and the spinal fluid have been repeatedly negative since 1928.

In spite of the fact that no abnormalities were found on physical examination, and because of the patient's complaints of pain in his knees, legs and toes, and of impotence, weakness and nervousness, he has received small doses of arsphenamine and silver arsphenamine and iodides by mouth. This treatment was given at long intervals, and the patient says it "peps" him up and makes him feel better.

A nodule was removed from the left buttock in February 1944. The mass measured 2 by 1.5 by 1 cm. It was extremely hard and was covered with ragged, fibrous attachments. On attempting to cut the nodule it was found to be composed of material of calcium density. The cut surface showed it was composed of whorls of fibrous-like tissue alternating with whorls of stony hard, white, calcified tissue. It was not until October, eight months later, that the microscopic examination was reported. The tissue was extremely hard and required prolonged decalcification. This resulted in the disappearance of most of the few cellular elements which remained in the calcified mass. However, a few normal-appearing nerve and blood vessels running through the center of the mass could be made out. Dense bands of collagenous connective tissue were seen coursing through the tissue and surrounding the areas of calcification. The nature or cause of the calcification could not be determined, but the appearance of the tissue was compatible with the history of injection of heavy metals into the gluteal region, although none of the material could be made out in the specimen. The presence of nerve fibers within the mass, it was felt, could well account for the history of pain in this region. The diagnosis was calcification of the gluteal region (following injections of heavy metals?).

#### DISCUSSION

DR G. F. MACHACEK: I am inclined to think that this is a real bone tumor, which I have seen in similar cases.

DR ISADORE ROSEN: I agree with the diagnosis as presented. I have seen all kinds of infiltrations following the injection of the various insoluble prepara-

tions of mercury, but I have never seen such an extensive, hard, bonelike infiltration as this patient presents

DR F PHILIP LOWENTISH Injections of a preparation of mercury were given between 1925 and 1928, about one hundred and fifty in all

**Sarcoid (Healed) of Skin, Lungs, Bones, Larynx and Kidneys?** Presented by DR BEATRICE M KESTEN

C R, a Negro woman aged 35, a domestic servant, born in New York city, is presented from Vanderbilt Clinic with an eruption of the face, the hands, the forearms and the right elbow of fifteen years' duration. The patient was admitted to Presbyterian Hospital on Nov 3, 1937, for progressive cutaneous lesions which had been present for the previous seven years. The eruption began with acute pain and swelling of the distal phalanges successively and spread to the entire hands and lower aspect of the forearms. Four years ago pimples developed about the mouth and the nose and continued to envelop the orifices. Similar lesions developed about the eyelids ten months ago. Eleven months ago the patient began to complain of malaise, fatigue and cough, and she has recently become hoarse, and swelling of the ankles has developed.

Examination showed numerous discrete, erythematous, firm, slightly tender papules on the eyelids, the nose, the lips and the chin. In addition, there were deep erythematous nodules about the nares, covered with crusts. The fingers were spindle shaped and covered with nodules which were discrete, firm and slightly tender. These extended onto the backs of the hands and were scattered over the forearms and the right elbow. There was a stricture of the pharynx and destruction of the epiglottis, the cervical nodes were enlarged, the lungs were clear, the heart normal, the liver enlarged, and edema of the ankles was present.

In 1937 tests with old tuberculin elicited negative reactions in dilutions of 1 10,000 and 1 1,000. The sputum was negative for tubercle bacilli. A biopsy from the right nostril contained numerous tubercles composed mostly of epithelioid cells without necrosis. A guinea pig inoculated with a nodule from the nostril did not contract tuberculosis. Roentgenologic examination of the chest showed dense hilar shadows suggestive of bilateral hilar adenopathy. There were increased bronchovascular markings in the lower lung fields. Roentgenograms of the hands showed sharply circumscribed oval defects in the proximal phalanges and in some of the middle and distal ones. There was cystlike degeneration in the styloids and the fifth right and the first left metacarpal bone. The feet showed similar but less advanced changes. The rest of the skeleton was normal except for slight generalized decalcification.

The results of blood studies were as follows. The hemoglobin was 70 per cent, erythrocyte sedimentation rate 75 mm in one hour. The serum protein was 89 cm per hundred cubic centimeters, albumin, 37 Gm, globulin, 52 Gm, nonprotein nitrogen, 32 mg, serum phosphatase, 32 Bodansky units, phosphorus, 28 mg, calcium, 12 mg, sodium, 127 milliequivalents, potassium, 45 milliequivalents, cholesterol, 338 mg, chlorides, 590 mg, and carbon dioxide, 60.7 volumes per hundred cubic centimeters. There were 4,600 white blood cells with 11 per cent eosinophils.

The urine showed 1 per cent albumin, with a few granular casts.

The course and treatment were as follows. The patient was placed on a high protein, high caloric, high vitamin and salt-poor diet, with added cod liver oil and wheat germ, and was permitted only light work. The lesions on the nose were removed by desiccation. In November 1939 the serum phosphatase was 139 units, the cholesterol 213 mg and the chlorides 612 mg per hundred cubic centimeters. Roentgenograms of the hands showed no new lesions, the cysts in the styloids had disappeared and all of the foci appeared a little smaller, with the surrounding bone of better density. The lung fields were clear, and by May 1940 all the cutaneous lesions had disappeared.

In May 1940, reactions to tests with old tuberculin were negative in a dilution of 1 1,000,000 and positive in a dilution of 1 100,000 (1 cm erythema with induration). Since May 1940 the tuberculin test has remained positive. A test with a dilution of 1 1,000 in September 1944 resulted in a bulla 3 cm in diameter with a deep induration.

Reexamination of the chest in September 1944 showed it to be clear. Roentgenologic examination of the hands and feet in October 1944 showed no further change from 1939.

The skin has remained clear, there has been no edema of the ankles, but the patient remains hoarse.

**Miliary Lupoid of the Face Generalized Lichenoid and Eczematoid Dermatitis Resembling Mycosis Fungoides** Presented by DR. GERALD F. MACHACEK

S. M., a Negro woman aged 33, is presented from Vanderbilt Clinic with a generalized eruption of four years' duration. This began as a few reddish macules on the left side of the chest and spread gradually to involve the entire body over a period of several months. At first there was no itching. The patient's private physician gave her injections in the hip and drops to take in water, but these were without benefit. She had no local treatment or roentgen irradiation before coming to the Vanderbilt Clinic. When healed, the macules left pigmented spots. The patient sought treatment at Vanderbilt Clinic in January 1944, and she states that she was somewhat helped by a series of roentgen irradiations, but otherwise continued to get worse. On July 14 she was admitted to Presbyterian Hospital, at which time the skin of the entire body, except the face, was involved. The eruption was a hyperpigmented, lichenified dermatitis with a tendency to bizarre contours. There was no oozing, but slight fissuring and maceration were seen between the toes. The hair of the scalp was thin, and a few patches of lichenification were noted on the scalp. The palms and the soles showed thickening and some pigmentation. There was a generalized adenopathy.

The patient's condition grew steadily worse in the hospital. Mild local treatment was given, with a course of typhoid injections, vitamin supplements and injections of crude liver. The skin of the axillae began to ooze, and the lichenified areas began to show infiltration. No gross abnormalities were noted in any studies.

Before the patient came to the hospital a biopsy specimen was reported as indicating psoriasiform dermatitis, another biopsy specimen taken from an infiltrated lesion on the back while she was in the hospital indicated "lymphoblastoma (mycosis fungoides)." Roentgen rays in fractional doses were then given to the entire body, in addition to the mild local treatment. The patient's condition improved slowly, and she was discharged in the fifth month of hospitalization, at which time the skin of the face and the ears was still oozing slightly. The biopsy specimen taken at this time from an area near the lower lip was reported as indicating "tuberculosis cutis."

The laboratory data were as follows. On July 16, 1944, hemoglobin was 11 Gm (76 per cent). There were 3,500,000 red blood cells and 8,800 white blood cells. Neutrophils were 58 per cent, lymphocytes, 30 per cent, eosinophils, 7 per cent, monocytes, 4 per cent, and basophils, 1 per cent. On July 17 the blood arsenic was 0.02 mg per hundred grams of dry blood. On July 19 the plasma vitamin C was 1.3 mg per hundred cubic centimeters. On August 4 a roentgenologic examination of the chest showed no abnormalities. On September 29 there were 10,300 white blood cells. The neutrophils were 51 per cent, the lymphocytes, 41 per cent, the monocytes, 7 per cent, and the eosinophils, 1 per cent. On September 30 cultures from the lesions on the lids yielded hemolytic *Staphylococcus aureus*. On October 2 a roentgenogram of the chest revealed no abnormalities. On November 10 the hemoglobin was 12.8 Gm. There were 3,900,000 red blood cells and 9,650 white blood cells. Neutrophils were

70 per cent, lymphocytes, 18 per cent, monocytes, 4 per cent, eosinophils, 7 per cent, and basophils, 1 per cent. Reactions were negative to tests with old tuberculin, in a strength of 1 1,000,000 on November 10, of 1 10,000 on November 13 and of 1 1,000 on November 17. On November 29 the hemoglobin was 11.5 Gm. The neutrophils were 81 per cent, the lymphocytes, 13 per cent, the eosinophils, 5 per cent, and the monocytes, 1 per cent.

Five urinalyses revealed no abnormality. Tests for cutaneous allergy were performed but were not helpful.

#### DISCUSSION

DR A BENSON CANNON. This patient was first believed to have a generalized exudative type of dermatitis, especially because of the extensive exudation and crusting. On admission, routine roentgenograms of the chest disclosed active tuberculosis of the lungs, so much so that we thought that the patient should be isolated. The eruption changed, became lichenified, a melanoderma developed, and there were lichenoid patches and thickening of the soles and palms and persistent swelling around the eyes. It made us think of an arsenical dermatitis, and the blood did show about four times the normal content of arsenic. The patient was given calcium and sodium thiosulfate, injections of typhoid bacilli, irradiation and other remedies, nothing helped her a great deal. She had an acute exudative eruption of the side of the cheek and chin, and this we were unable to diagnose clinically. Dr Machacek said that it finally showed characteristic tuberculosis histologically. I am wondering whether, on the basis of tuberculosis of the lungs and the skin, the condition could not fit into generalized exfoliative tuberculosis, rather than mycosis fungoides.

DR MAURICE J COSTELLO. On several occasions patients have been shown before this section who have had pityriasis rosea-like eruptions, or lichen planus, from the administration of the arsphenamines. The fact that there was an exacerbation of the pulmonary tuberculosis after the injection of arsphenamine would substantiate that opinion.

#### Chronic Lymphangitis and Chronic Recurrent Angioneurotic Edema of the Face Presented by DR F PHILIP LOWENFISH

L. S., a white man aged 45, is presented from Vanderbilt Clinic complaining of swelling of the face of fifteen years' duration. About fifteen years ago, after and acute attack of erysipelas of the face which healed in about ten days, the upper lip was left swollen, and it has remained so since that time. The patient thinks that it gets larger and then smaller at times, but it has never even approached normalcy. The huge, boggy swelling hanging under the chin for the same length of time has apparently receded considerably during the past two months. About six weeks ago a pinkish edema of the upper right eyelid appeared, and this has remained fixed. The patient has had recurrent edema of the upper eyelids for many years. The upper lip is enlarged, thick and rubbery, and juts forward somewhat like the peak of a cap.

The laboratory data are as follows. Wassermann and Kline reactions of the blood were negative. A complete blood count and sedimentation rate were normal. Roentgenograms of the frontal, ethmoid and sphenoid sinuses were clear.

The patient has had twenty teeth extracted, including all from the upper jaw and a few from the lower jaw. A series of staphylococcus toxin injections has been given, and about three months ago he received a course of 1,280,000 units of penicillin given intramuscularly (20,000 every three hours for eight days). His condition has remained unimproved, and he is now receiving filtered roentgen ray therapy to each side and to the under surface of the upper lip. Up to the present time he has had six treatments given a week apart of 150 r each (65 kilovolts, 20 milliamperes, filtered through 2 mm of aluminum and at a distance of 14 cm).

The patient is presented for suggestions as to further treatment.



## DISCUSSION

DR ISADORE ROSEN The only therapy that I can suggest is plastic surgery

DR MAURICE J COSTELLO We have treated at Bellevue Hospital a number of patients whom we cannot say were permanently cured, but who were certainly greatly improved while the sulfonamide drugs were administered. I think success is more likely to occur if the sulfonamide drugs are continued for a long period of time.

## A Case for Diagnosis (Lipoidosis?) Presented by DR PAUL GROSS

N I, a man aged 19, was seen at the Hospital for Joint Diseases because of an extensive cutaneous eruption which he had first noticed eight months ago. The first lesions to appear were nodes on his fingers. These increased greatly in size and number but caused no discomfort. Except for measles, there was no history of previous illness.

On the second, third and fourth fingers of the right hand and on the left index finger are nodules of a bluish red color and rather firm consistency. They are located near the finger joints, and the largest ones are about the size of a pea. They are freely movable and not tender. On the extensor surface of the forearms in juxta-articular position to the elbows there is a larger nodule, about the size of a cherry, subcutaneous and covered by normal skin. The entire pubic area is covered with reddish brown papules with a rounded top which shows slight scaling. These papules are the size of a large pinhead, densely arranged but not confluent, and form a pattern resembling a lichen moniliformis. There are many small, discrete, translucent papules of a yellowish pink color in both armpits and on the pinnae of the ears. There is an acneiform eruption on the chest and upper part of the back, and an erythema and minute papules in the nasolabial folds. A few whitish, flat, papular lesions are seen on the buccal mucosa corresponding to the last molar.

Roentgenograms of both hands revealed moderately advanced arthritic changes in the interphalangeal joints. Circular defects were present in the juxta-articular ends of the small bones, suggestive of gout. There were also arthritic changes in both wrist joints. The lateral views of the elbow joints were radiographically normal.

There was no albumin or sugar in the urine. The Kahn and Kline reactions of the blood were negative. A blood count revealed no pathologic changes. The sedimentation rate was 8 mm in forty-five minutes. A blood chemistry study showed 93 mg sugar per hundred cubic centimeters and a total cholesterol of 102 mg per hundred cubic centimeters, of which 32 mg was free cholesterol.

## DISCUSSION

DR FRED WISE If I am not mistaken, only 4 or 5 bona fide cases of extracellular cholesterosis are described in the literature of today. No special stains for fat were made in this case, but if sections were properly stained for fats, the histologic picture of extracellular cholesterosis might be demonstrated in sections from one of the lesions on the hand.

DR EUGENE T BERNSTEIN In my opinion the diagnosis can readily be made on clinical grounds, particularly on morphologic attributes. I have no doubt that a histologic examination would confirm the diagnosis. The lesions seen on the patient show transitional shades from chamois yellow through brown to a dusky red. On the left ear one could see the typical chamois hue of xanthoma. On the elbows the lesions have a brownish discoloration, whereas the lesions on the hands are dusky red. It seems to me that we are dealing with a metabolic disturbance of lipids, a picture similar to that described in extracellular cholesterosis. Tannhauser, an authority on lipid metabolism, thinks that the designation of extracellular cholesterosis should be disregarded and replaced by the more embracing diagnostic term, lipoidosis. This case presents an example of such an instance.

DR PAUL GROSS On clinical grounds, we were in favor of the diagnosis of extracellular cholesterosis. The case reminded us of a patient presented by Dr Oscar Levin before this section, who showed a similar array of lesions. At that time Dr Bernstein doubted this diagnosis. The pathologic findings of the sections obtained by biopsy from the skin of the pubic region in this case make it difficult to maintain the diagnosis of extracellular cholesterosis. The presence of many giant cells deviates from the description given by Urbach. The results of stains for fat should decide whether we are dealing with an unusual type of lipoidosis. The low total cholesterol in the blood of our patient resembles the findings in Urbach's case, except for the normal ratio of free and esterified cholesterol in our case.

NOTE—On the basis of several biopsies, the diagnosis of lipoidosis can be ruled out. The histologic changes are so unusual that a definite diagnosis cannot be offered at present. The sections were studied by Dr Jaffe and Dr Lichtenstein and were examined by Dr Machacek, and the description of the pathologists was as follows:

A specimen obtained from the skin of the pubic region showed that the epidermis was atrophic in the affected areas. In the cutis one observed vascularization, clumps of peculiar foreign body giant cells and collections of small mononuclear cells dispersed around vascular channels. A second specimen from the same region showed some fibrosis in the subpapillary zone of the corium, increased vascularization and the presence around some of the vessels of chronic inflammatory cells. There were occasional giant cells, present, but not nearly as many as were seen in the previous specimen. A sudan stain showed the presence of lipid within some of the connective tissue cells, but on the whole the lesion contained comparatively little lipid.

Sections of an extirpated nodule on the fingers showed essentially the same process. Within the superficial and deeper layers of the cutis there were collections of cells apparently of the nature of leukocytes, and numerous multinuclear giant cells. There was evidence to suggest that these cells were derived from the reticuloendothelial cells of blood vessels. There was no appreciable amount of lipid in the lesion as seen in sudan stain, and chemical analysis of a slice of tissue likewise failed to reveal any lipid. In another lesion there were observed conspicuous collections of blood vessels, considerable fibrosis and also a partial infarction.

#### A Case for Diagnosis (Nevus?) Presented by DR LOUIS CHARGIN

A B, a man aged 24, had an eruption of the left side of the face some six years ago. The eruption spread rather rapidly, so that in a space of several months it extended to the present dimensions. He has been treated by several physicians with local remedies without the slightest effect. The patient has diabetes, takes insulin and is under good control.

Occupying the left cheek, the left ear, the jaw and the adjacent neck there is a papular eruption which is irregularly distributed over the affected areas, the border being irregular in outline. It is dark red, slightly scaly in part, but mostly smooth and shiny. Superficial examination gives the impression of lupus vulgaris, but on diascopy there is no suggestion of tubercles nor is there any reason for a diagnosis of lupus erythematosus. There are no subjective symptoms.

Biopsy showed the epidermis to be considerably acanthotic, with the palisade layer intact. The surface was verrucous, covered by a densely laminated horny layer. In the subepidermic region the vessels were dilated, and about them was a moderate small round and wandering connective tissue infiltration. There was a slight increase in mast cells, but not enough to make a diagnosis. The elastic tissue was unchanged. There was no evidence of epithelioid cells or of tubercles,

and no evidence of lupus vulgaris. It was felt that the picture might possibly fit in with a nevus.

#### DISCUSSION

DR A. BENSON CANNON. I could not make a better diagnosis than Dr Chargin's, but I don't know that I should have thought of nevus either from the clinical appearance or from the age of the patient. I have never seen a nevus develop in a man 20 or older, and I believe he has had the lesion only six years. I had occasion to look up the literature, and the oldest patient whom I found was 13 when the nevus developed. I should think from the lesions on the scalp and face that it might be explained as psoriasis, although the histology has no resemblance either to psoriasis or to nevus.

DR FRED WISE. A diagnosis of nevus is hard to accept because of the diffuse, widespread scaling eruption on the entire scalp. If one examined the scalp alone the thought of nevus would not occur. The scalp lesion resembles psoriasis or seborrheic eczema, but the presence of a linear lesion on the nose and the sharply bordered lesion on the neck lead one to consider a nevus or a nevroid disease.

DR CHARLES WOLF. One cannot be overinfluenced by the biopsy report here, but on clinical grounds there are enough objective signs to consider it in the group of a psoriasiform eruption. The clinical data supporting the diagnosis are these. First, there are sharply demarcated lesions in the scalp with normal skin interrupting the affected areas. There are micaceous, silvery scales which could be removed, eliciting pinpoint hemorrhages. Furthermore, the man has stippling of one of the nails. It is well known that psoriasis may for many years be represented by a solitary lesion. As time goes on, other lesions may develop. I would therefore tentatively say that it is psoriasis. The biopsy revealed acanthosis, which is one of the definite features of psoriasiform pathology.

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*Feb 19, 1945*

**Unilateral Acrodermatitis Chronica Atrophicans** Presented by DR. GERALD FRANK MACHACEK

H. W., a white woman aged 50, began to have lesions following sunburn five years ago which now involve the right forearm and part of the right arm throughout most of the circumference. These are erythematous, atrophic and on palpation firmer than normal cutaneous tissue. The two radial pulses are equal.

Roentgenologic examination of the cervical region disclosed no cervical ribs. Histologic examination confirmed the diagnosis of acrodermatitis chronica atrophicans.

#### DISCUSSION

DR. JOSEPH C. AMERSBACH. I cannot give much help as far as treatment is concerned. I agree with the diagnosis.

DR. J. LOWRY MILLER. The interesting feature is the unilateral characteristic. There is a history of having pain in the same side of the neck previous to the onset of the eruption. The patient received diathermy treatment for the pain. A cervical rib was thought of at the first visit to the clinic as a possible cause of the pain and subsequent eruption, but this has been ruled out by roentgenologic examination.

DR. MAURICE J. COSTELLO. It is an unusual and interesting case. For practical purposes one may say that the disease is unilateral. I believe she has begun-

ning changes on the other arm. They are faint enough, I admit, and would not have been suspected if she did not have frank lesions on the right forearm and arm.

DR RICHARD J KELLY I think that the patient should be investigated carefully from the standpoint of a thyroid deficiency, and I am interested in knowing whether there is any difference in blood pressure between one upper extremity and the other. I suppose a roentgenogram of the chest has been made.

DR ROYAL M MONTGOMERY The unusual feature in this case is the fact that the eruption is unilateral and limited only to the right arm. I doubt whether the severe sunburn mentioned in the history has anything to do with the causation. If the sunburn were equally distributed, both arms should be affected.

DR GERALD F MACHACEK I think the suggestion of checking blood pressure in both arms is a good one. The pulse was felt in both radial arteries, and the two seemed to be equal. A roentgenologic examination disclosed no sign of a cervical rib. Once in a while instead of a cervical rib there is present a band of fascia across the brachial vessels and cervical plexus, which gives the same symptoms as a cervical rib but which cannot be felt and cannot be seen by roentgenologic examination. The patient complains of pain in the third and fourth fingers of the right hand.

**A Case for Diagnosis (Rosacea, Rosacea-like Tuberculid?)** Presented by DR J LOWRY MILLER

J S, aged 42, was first seen at the clinic of the New York City Hospital, in January 1945. He complained of an erythematous eruption present on his face for twenty years. He stated that it began as acne during puberty but has been present for twenty years. No treatment of any kind has been given. Aside from an operation to remove a bony spur which was causing pain in his leg and numbness in his foot, he has enjoyed good health.

Examination shows numerous pea-sized red macules and papules scattered over the entire face. One papulopustule is present. Telangiectases are seen in many of the lesions.

Roentgenograms of the bones of the legs revealed changes suggestive of Paget's disease of the bone. Histologic examination of the lesion from the forehead established a diagnosis of rosacea and showed no changes suggestive of a tuberculid.

DISCUSSION

DR JOSEPH C AMERSBACH I believe this is rosacea. The lesions do not strike me as being of the Lewandowski type. I do not know how much specific therapy has been instituted or what the diet has been.

DR MAURICE J COSTELLO I think that the patient has rosacea, in spite of the fact that he has had it so long. I think that it is unusual to have rosacea persist so long without remission. The man is a heavy coffee drinker. If he is asked to follow a diet for patients with rosacea and if dilute hydrochloric acid is administered the eruption should improve, but I am inclined to think that he is going to have rosacea indefinitely.

DR RICHARD J KELLY I believe this is rosacea. There is a possibility that the patient may have had a juvenile acne. However, at present the characteristic features of the eruption place it in the category of rosacea. There is a definite history of ingestion of strong coffee.

DR GERALD F MACHACEK My impression also is that it is probably rosacea. However, I think another biopsy should be performed on a good fleshy nodule as it is possibly a rosacea-like tuberculid. I examined one biopsy specimen, and that showed only chronic inflammatory changes. That in no way eliminates the possibility of a tuberculid.

DR ROYAL M MONTGOMERY In view of the fact that he has had the rosacea so long, I suggest a course of bismuth subsalicylate. Some patients with rosacea respond to this type of therapy.

James Lowry Miller, M D, *President*

Leslie P Barker, M D, *Secretary*

*March 19, 1945*

**Subcutaneous Recurrent Effusion** Presented by DR GERALD F MACHACEK

A P, white, aged 43, presents on the outer aspect of the right thigh a diffuse swelling extending from the middle of the upper third to almost the knee. There is at present no discoloration except for a scar in the middle of the thigh where there originally was an infected lacerated wound which was superficial. On Feb 1, 1945, the patient suffered an extensive contusion of the right thigh with laceration. There was discoloration which resulted two weeks later in subcutaneous liquefaction. On palpation, a soft boggy mass in which a fluid wave was elicited, was present. This was aspirated, and 2½ ounces (70.9 Gm) of somewhat turbid straw-colored fluid was obtained. One week later a smaller fluctuating mass was present near the knee. One ounce (28.3 Gm) of turbid yellow fluid was obtained on aspiration. Two days ago, there was a reaccumulation of liquid which again extended from the region of the hip to the knee. No elevation of temperature or tachycardia was present. The patient is comfortable, being merely upset by the formation of this elongated liquid-filled mass, with soft fluctuant walls.

**DISCUSSION**

DR J LOWRY MILLER I believe that the effusion results from an inflammation of the sheath of the vastus lateralis. There is a history of injury in this area. I should suggest aspiration of the fluid and injection of 5 per cent phenol solution as a method of treatment.

DR JOSEPH C AMERSBACH I feel, as Dr Miller suggested, that it is a condition resulting from a hematoma and possibly an inflammation of the vastus lateralis and should suggest incision leaving a drain in the site of the incision for probably a week or ten days. If this does not clear up following this procedure, I believe that the injection of some sclerosing solution would be of benefit.

DR RICHARD J KELLY This man had an injury and a definite traumatic hematoma. It was aspirated by Dr Machacek, cleared and recurred. I should suggest, if it is possible, that a guinea pig be inoculated. I should like to ask the presenter whether there is any arthrosis of the knee joint.

DR GERALD F MACHACEK I agree with the diagnosis of inflammation of the fascial sheath. The thing that puzzles me is whether it is or is not connected with some of the bursae of the knee, but I do not think that it is. I think that some sclerosing solution will have to be injected or some permanent drainage made.

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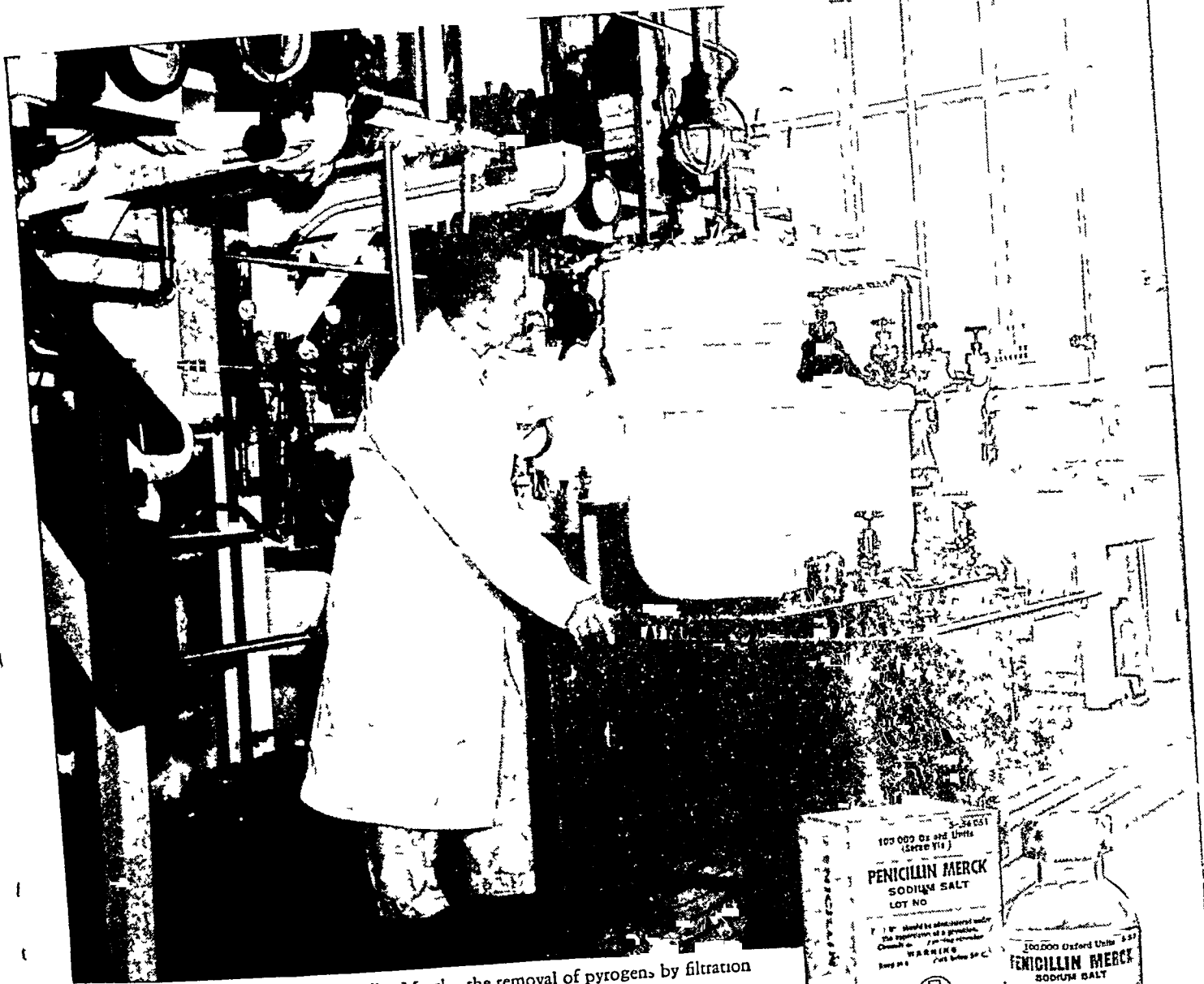
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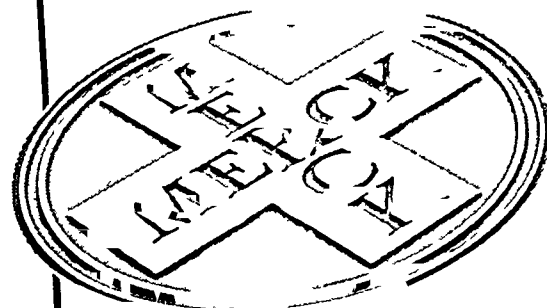
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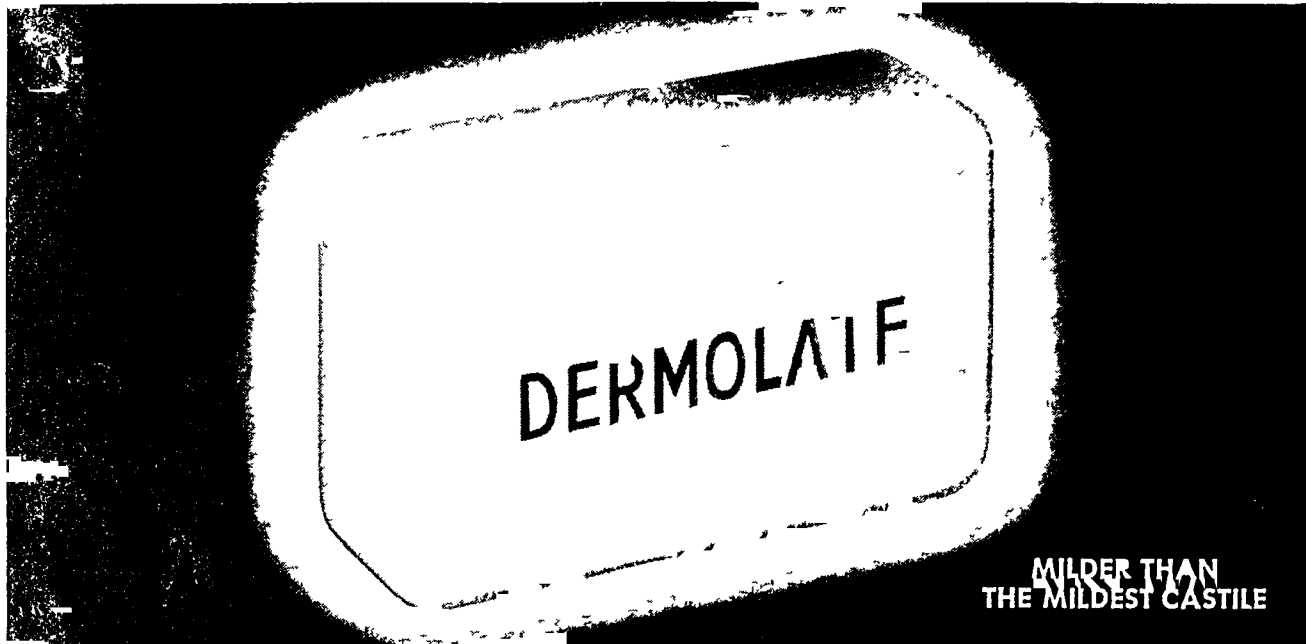
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<sup>1</sup> I. H. Blank, *Arch. of Derm. and Syph.* 39: 811-824 (1939).  
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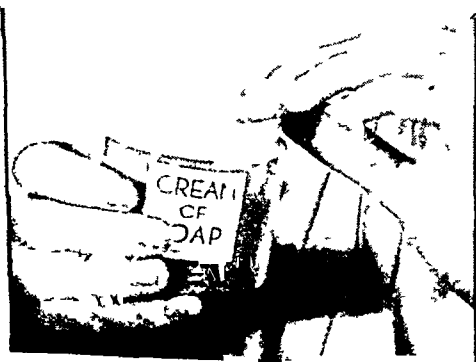


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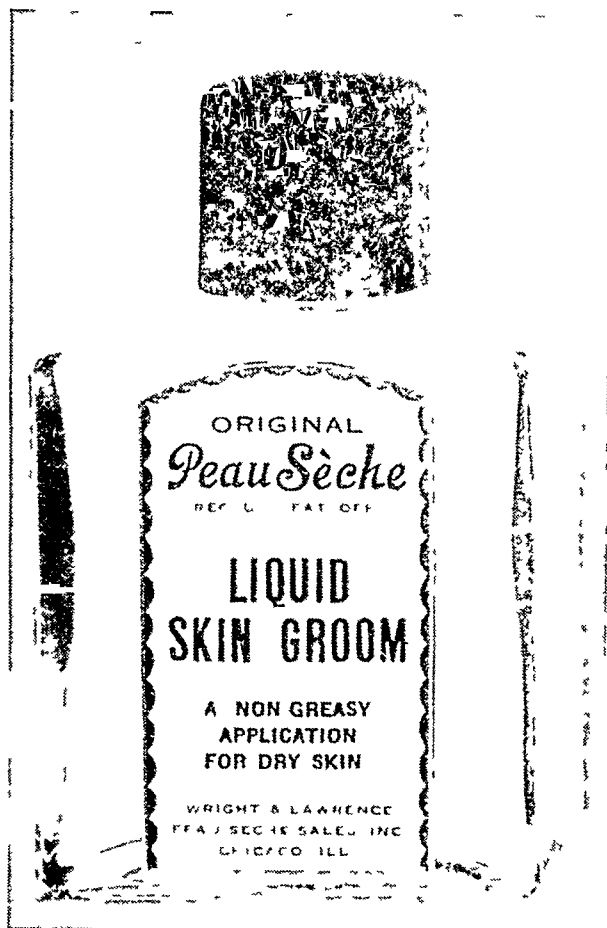
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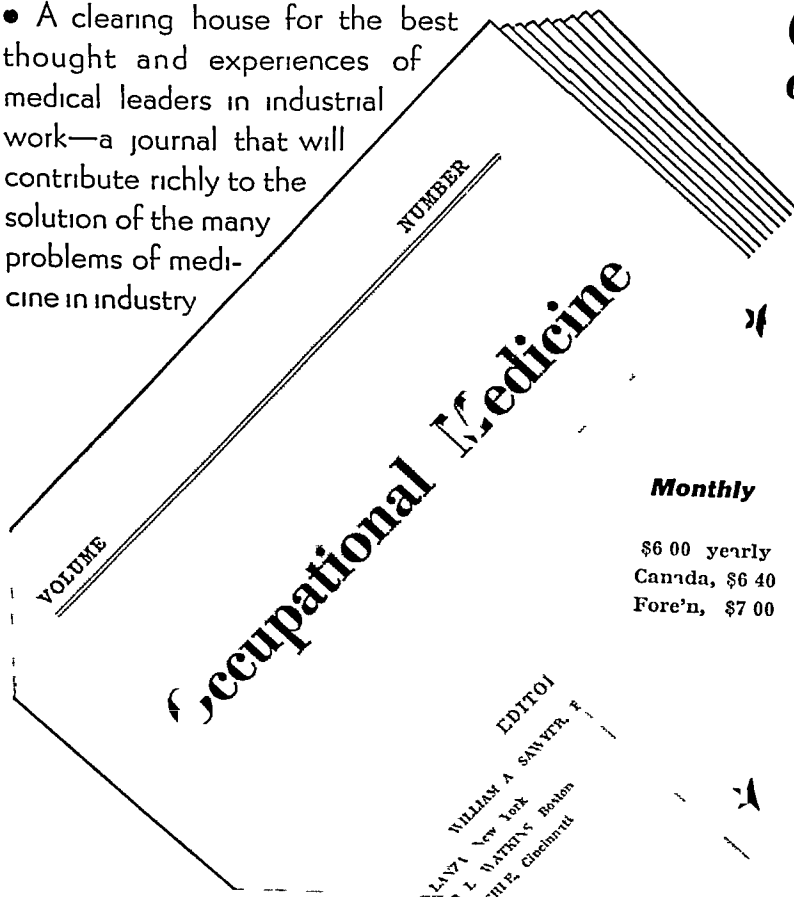
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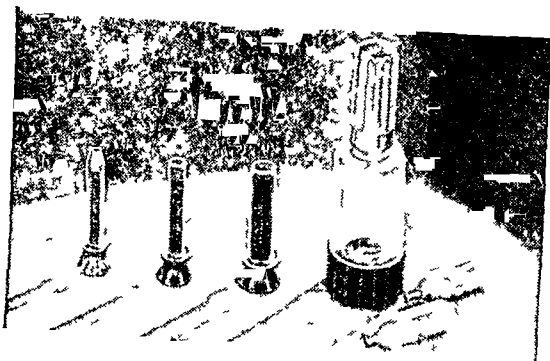
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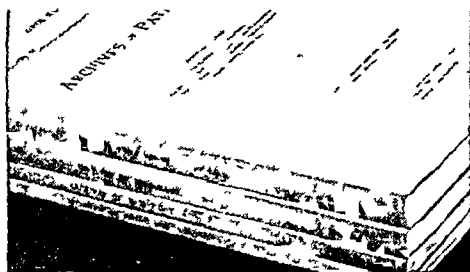
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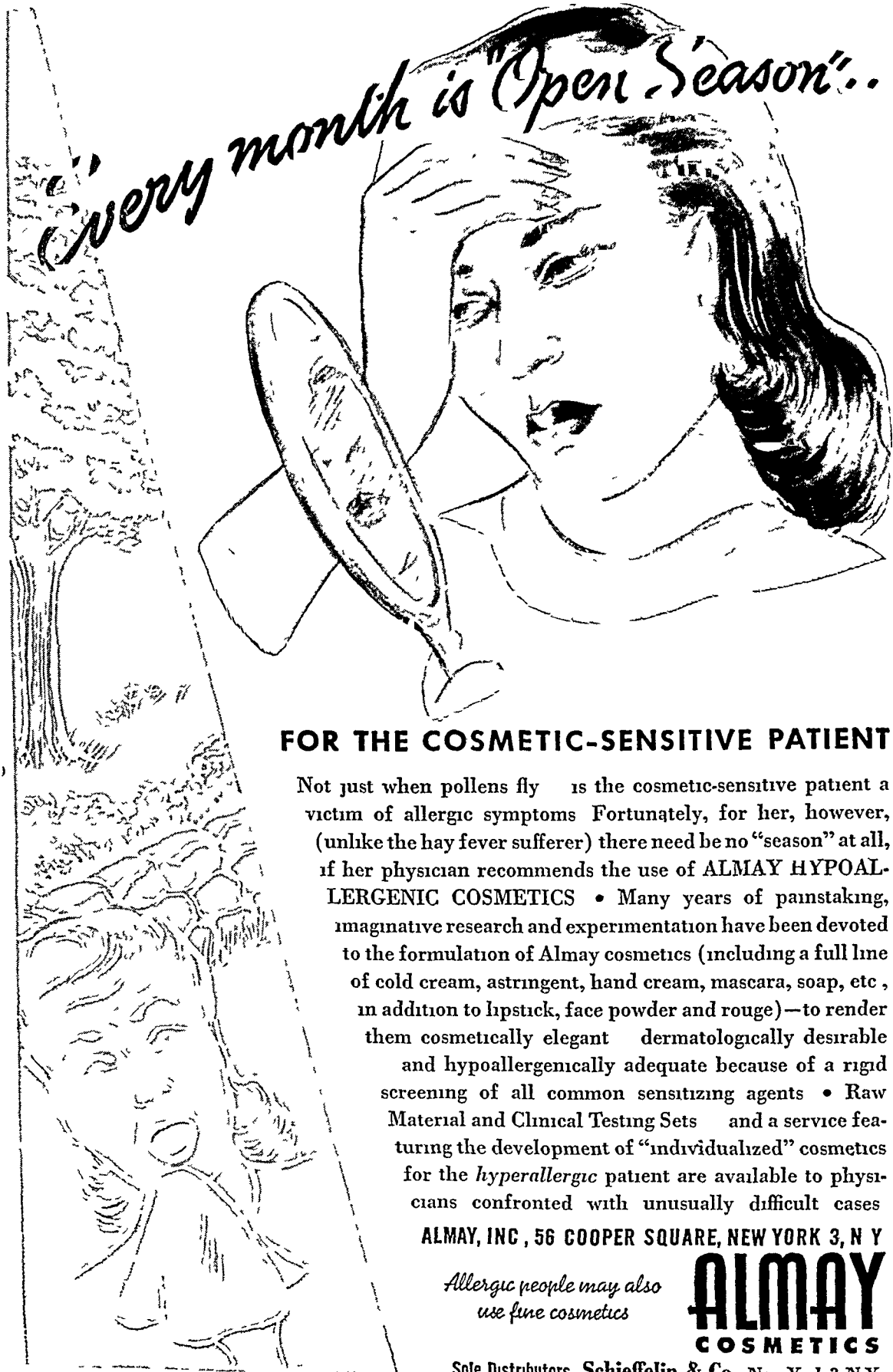
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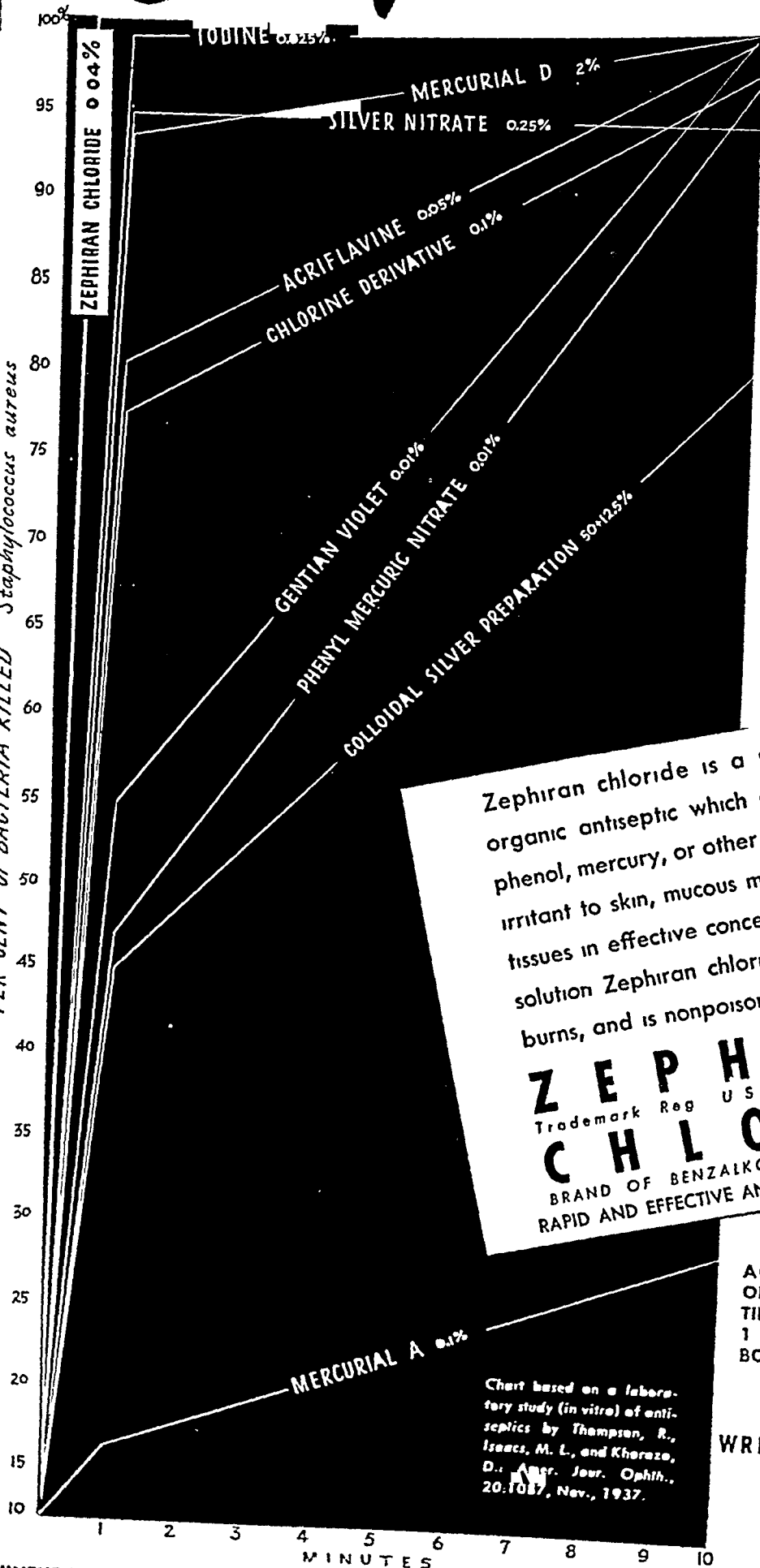
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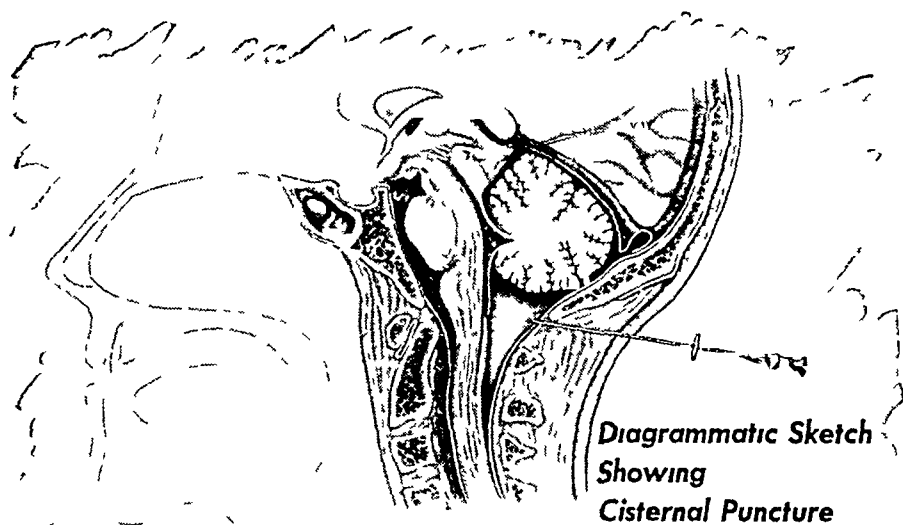
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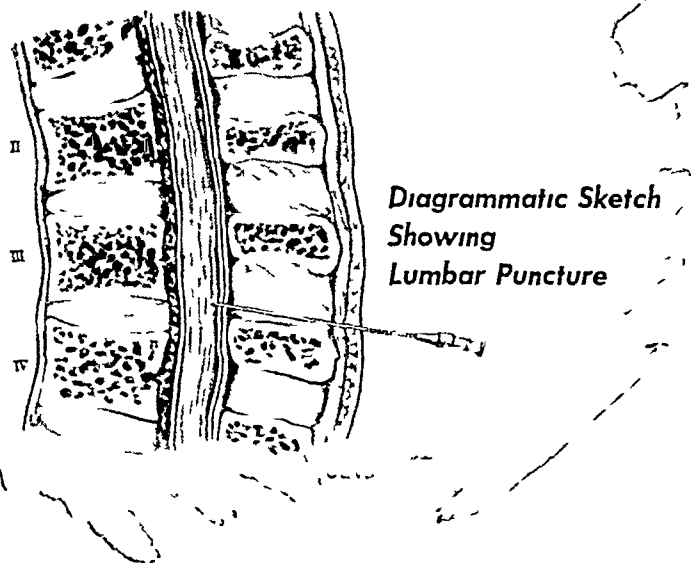
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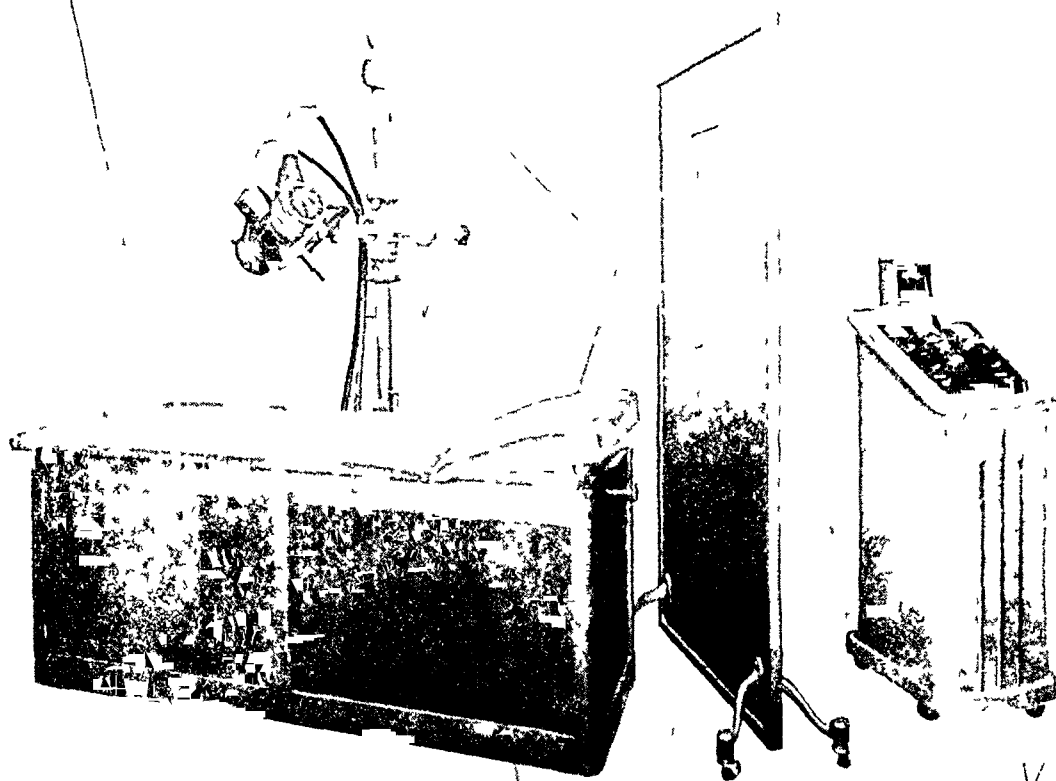
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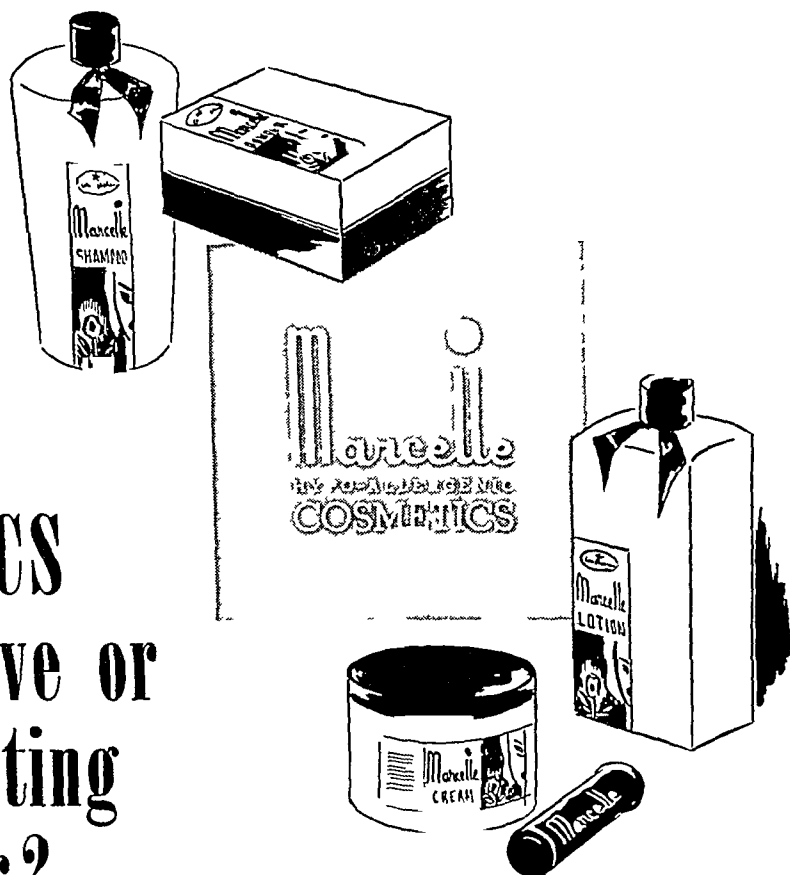
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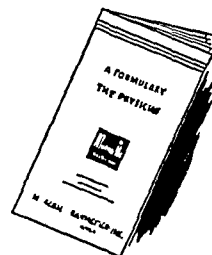
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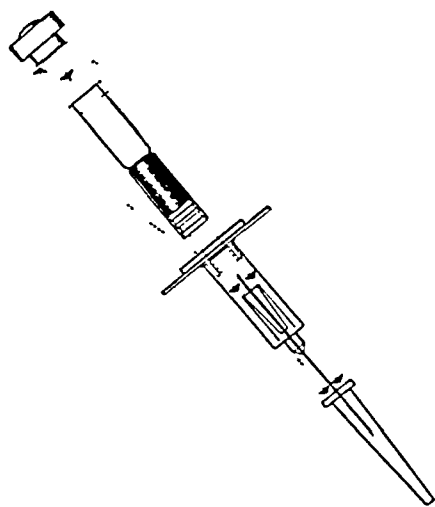
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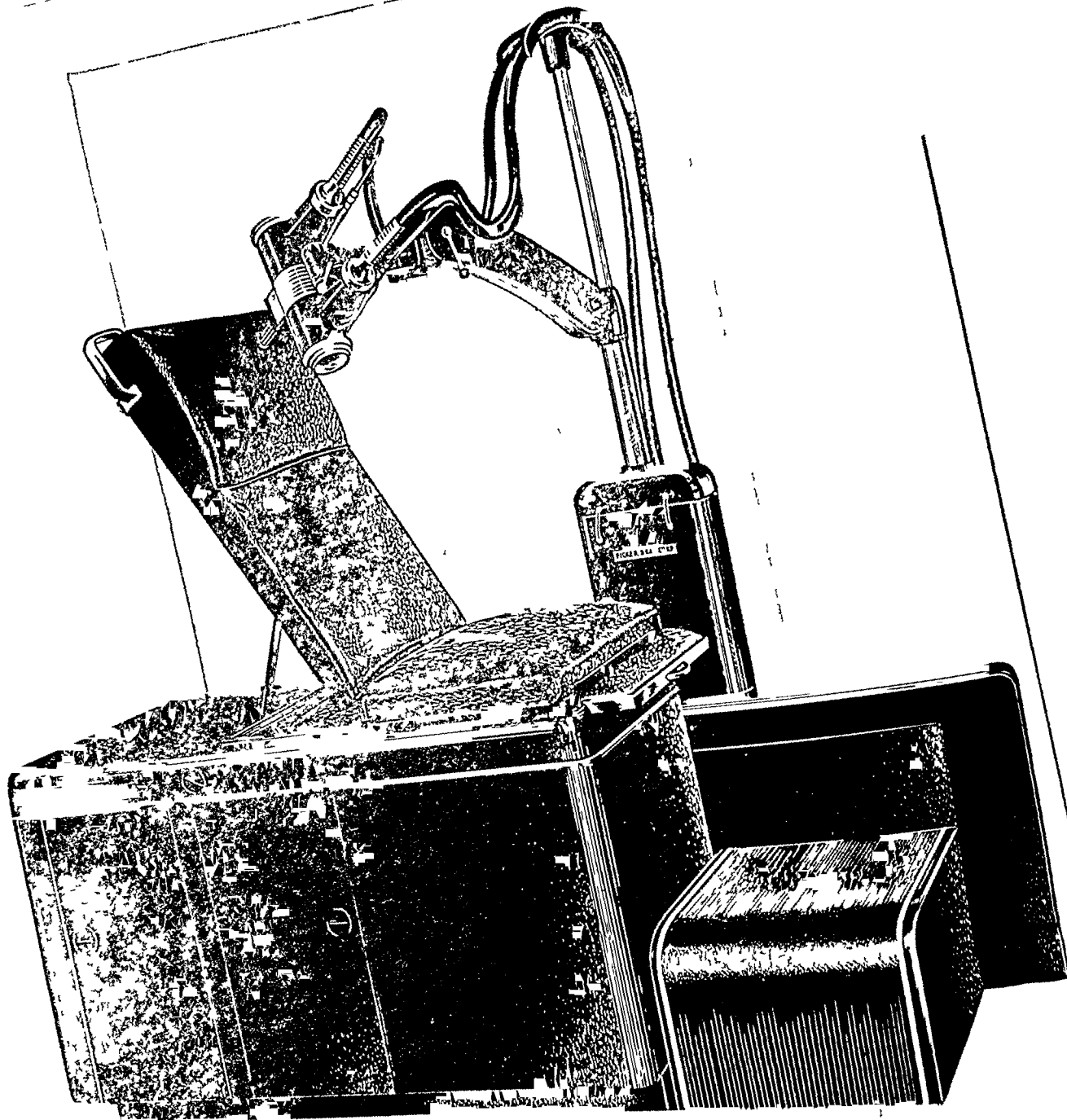
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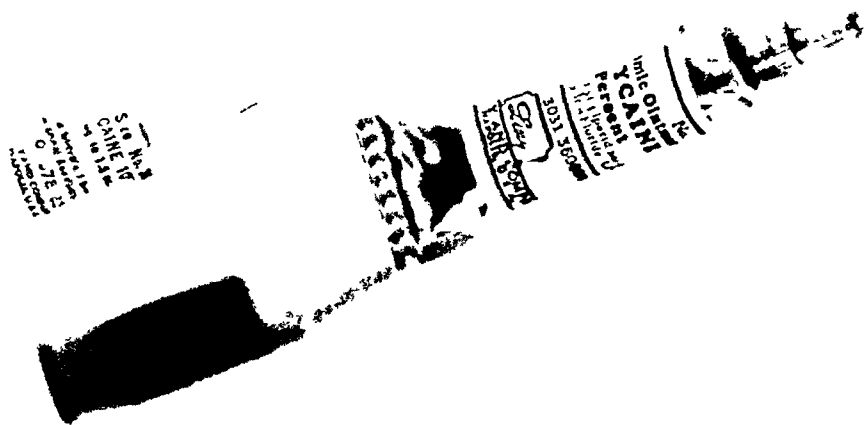
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# Archives of Dermatology and Syphilology

VOLUME 54

NOVEMBER 1946

NUMBER 5

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## VEHICLES IN TOPICAL DERMATOLOGIC THERAPY

Their Functions and Physicochemical Characteristics

C GUY LANE, M D

AND

IRVIN H BLANK, Ph D

BOSTON

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From the Department of Dermatology, Harvard Medical School, and Massachusetts General Hospital



## I INTRODUCTION

In the preparation of a dermatologic, therapeutic material for topical application, it is not uncommon for the vehicle to be given too little consideration. Custom too often determines the selection of the vehicle. Its choice may depend more on pleasing physical properties than on therapeutic efficacy. Such properties of a vehicle as odor, color, stability and compatibility with various drugs are emphasized. It is our belief that sufficient thought is rarely given to the functions which the vehicle performs or to such physicochemical characteristics of the vehicle as its ability to dissolve drugs, to cool the skin and to wet the skin.

In the literature, there are relatively few papers which correlate the various functions of vehicles with their physical and physicochemical properties or which discuss the physicochemical action of the vehicles on the skin. There is one German monograph on this subject by Czetsch-Lindenwald and Schmidt-LaBaume,<sup>1</sup> but no similar text in English has come to our attention. There has been considerable investigation of the action of specific drugs in various vehicles, such as the recent series of papers by Strakosch,<sup>2</sup> each of which contains a complete bibliography.

In the choice of a vehicle, one may need to consider (1) the general characteristics of the patient's skin—e g, whether it is oily, dry, light, dark, "thin" or "coarse", (2) the area of skin being treated—e g, whether it is hairy or glabrous, (3) the kind of lesions present—e g, oozing or hyperkeratotic lesions, (4) the effect of the vehicle on the drug—e g, hydrolysis, oxidation or chemical combination, (5) the effect of the drug on the vehicle—e g, separation of an emulsion type of vehicle, (6) changes which occur in the vehicle after application to the skin—e g, evaporation or oxidation, (7) influence of the vehicle on the action of the drug on the skin—e g, increase in the penetration of the drug, and (8) action of the vehicle itself on the skin—e g, prevention of evaporation or emollient action.

For the purpose of this discussion, a therapeutic material for topical application is considered to be a vehicle containing one or more drugs. There are four ways in which a therapeutic material may act when applied to the skin.

1 Czetsch-Lindenwald, H., and Schmidt-LaBaume, F. *Salben und Salbengrundlagen*, Berlin, Julius Springer, 1937.

2 Strakosch E. A. *Studies on Ointments*. I Penetration of Various Ointment Bases, *J Pharmacol & Exper Therap* **78** 65-71 (May) 1943, II Ointments Containing Salicylic Acid, *Arch Dermat & Syph* **47** 16-26 (Jan) 1943, III Ointments Containing Sulfur, *ibid* **47** 216-225 (Feb) 1943, IV Local Action of Salicylic Acid Plus Sulfur from Various Ointment Bases, *ibid* **48** 384-392 (Oct) 1943, V Ointments Containing Resorcinol, *ibid* **48** 393-399 (Oct) 1943.

First, it may react chemically with the skin by such processes as direct chemical combination, oxidation or reduction. The exact chemical reactions of many drugs with the skin are not well understood, but much clinical experience has taught the physician how to use such substances as sulfur, salicylic acid, tar and boric acid. The vehicle, however, is not thought to undergo chemical reactions with the skin.

Secondly, if a drug penetrates the skin, it may directly alter the physiologic activity of the skin. If a specific alteration of a physiologic property of the skin is desired, however, it is more easily accomplished by ingestion or injection of the drug than by topical application (compare the action of pilocarpine when injected intramuscularly and when topically applied). The vehicle by itself seldom directly alters the physiology of the skin, but in so far as it may affect the penetration of the drug, it may indirectly influence the physiologic activity of the skin.

Thirdly, a topical application may cause an immune reaction to occur. There are few topical therapeutic procedures which depend on this type of reaction for their effectiveness. In fact, when such reactions do occur, as in the case of a contact dermatitis in which one of the topically applied substances is the allergen, it is an indication that such treatment should be stopped. When the therapeutic material is allergenic, either the drug or the vehicle may be the allergen, but rarely have immune reactions to vehicles been noted.

Fourthly, a topical application may produce a physicochemical effect. In fact, almost all therapeutic materials influence the skin in one way or another by virtue of their physical and physicochemical properties. A material which has a low boiling point will cool the skin when it evaporates, an occlusive covering will warm the skin by preventing normal evaporation of the sweat and retarding radiation of heat, an oily material will make the skin more "supple", an oil solvent will make the skin more "brittle". The physicochemical action of a therapeutic material is more likely to be determined by the vehicle than by the drug.

Thus, in topical, dermatologic therapy, the vehicle rarely undergoes a specific biochemical reaction with the skin, and physiologic and immune reactions to the vehicle are relatively unimportant, but physicochemical changes do occur each time a therapeutic material is placed on the skin. These physicochemical actions, which depend primarily on the vehicle, may be an important part of the entire action of the complete therapeutic material.

This review will discuss these physicochemical characteristics of vehicles and the various functions which the vehicles perform. It is hoped that a better understanding of these principles will aid the physician in choosing the correct vehicle in topical, dermatologic therapy,

## II CLASSIFICATION OF VEHICLES

It is often difficult to decide just what constitutes a drug and what constitutes a vehicle in any therapeutic material. One might argue as to whether the starch in a paste or the zinc oxide in a shake lotion is a drug or a part of the vehicle. So far as is now known such powders do not react chemically with the skin and do not directly alter its physiologic activity. They do exert physicochemical actions on the skin. Perhaps no sharp line can be drawn between drugs and vehicles in all pharmaceutical preparations. For the purpose of this discussion however, those materials which have a biochemical or physiologic action will be called drugs and those which are likely to affect the skin only physicochemically will be called vehicles.

In the following classification, this physicochemical action on the skin has been used to determine the position of the vehicle in the classification. We have chosen to classify the vehicles according to whether they act on the skin primarily as (a) an aqueous vehicle, (b) an oily vehicle, (c) a powder or (d) an organic solvent.

## A Vehicles which act as aqueous mixtures

- 1 Water
- 2 Shake lotions—e g, a mixture of zinc oxide and water
- 3 Gels of hydrophilic colloids—e g, bentonite jelly or surgical lubricant

## B Vehicles which act as oils

- 1 Water-immiscible oils—e g, petrolatum or olive oil
- 2 Water-miscible oils—e g, anhydrous wool fat
- 3 Oil in water emulsions—e g, vanishing creams
- 4 Water in oil emulsions—e g, hydrous wool fat
- 5 Pastes—e g, a mixture of starch and petrolatum
- 6 Collodions

## C Vehicles which act as powders

- 1 Hydrophilic powders—e g, starch
- 2 Hydrophobic powders—e g, talc or zinc stearate

## D Vehicles which act as organic solvents

- 1 Water-miscible solvents—e g, alcohol or acetone
- 2 Water-immiscible solvents—e g, ether

Physically, vehicles are liquid, semisolid (such as petrolatum) or solid. The preceding classification does not always distinguish between two vehicles of different states. For instance, olive oil and petrolatum would each be classified as a water-immiscible oil. Gels of hydrophilic colloids may be semisolid but nevertheless are classified as aqueous vehicles. The classification of many of those vehicles which are mixtures (emulsions, collodions) is determined not by the predominant characteristic of the vehicle as such, but rather by its characteristics after it has been on the skin for a while. An oil in water emulsion may contain 75 per cent water and have many of the characteristics

of water when it is applied to the skin, but soon after it is applied to the skin the water evaporates, and a film of water-miscible oil is left on the skin, after which the vehicle acts more like an oily vehicle than an aqueous one. A collodion often contains over 90 per cent of some organic solvent. After it is placed on the skin, however, this solvent evaporates, leaving behind a film of flexible collodion which will be shown to have many of the properties of a film of a water-immiscible oil. It is possible that both shake lotions and gels of hydrophilic colloids should be classified as powders rather than as aqueous vehicles, since a large part of the time they are on the skin they act more like powders than like aqueous mixtures.

### III PHYSICOCHEMICAL CHARACTERISTICS OF VEHICLES

For a better understanding of the functions of vehicles it is considered important first to review briefly some of the physical and physicochemical properties of vehicles.

*A Solubility of Drugs in Vehicles* The solvent action of the vehicle is important from three points of view. The major consideration is the ability of the vehicle to dissolve the various drugs which are incorporated into it. Of less importance, no doubt, is the ability of the vehicle to dissolve secretions of the skin. Finally, in a few instances, consideration must be given to the solubility of substances which may come into contact with the vehicle from the environment after the vehicle has been applied to the skin.

A vehicle may carry a drug in true solution or in mechanical suspension. It is probable that no substance is completely insoluble in any vehicle, but some substances are so slightly soluble that they may be considered insoluble for purposes of this discussion, and when placed in a vehicle in which they are insoluble they will be held in that vehicle as a mechanical suspension. There are two major types of solvents among the vehicles: aqueous and oily. There are, of course, many types of oils used as vehicles. Solubility of the drugs in the oils will vary, but in general, drugs which are soluble in water are sparingly soluble in oils, and vice versa.

The solubility of some of the commonly used drugs in various solvents is shown in table 1. Solubility as a rule increases with the temperature. For the purpose of simplicity, the temperature factor is omitted from this table; all solubilities shown are for temperatures between 20 C and 30 C—the approximate range for room and skin temperatures.

The ability of the vehicle to dissolve skin secretions and the protection the vehicle offers from air-borne substances need not be discussed here, since they will be considered as specific functions of the vehicle when applied to the skin.

TABLE 1—*Solubility of Drugs in Various Vehicles*

Drug	Vehicle		
	Water	Ethyl Alcohol	Miscellaneous
Boric acid $H_2BO_3$	6.65 Gm /100 Gm water *	6.85 Gm /100 cc sol †	Glycerine 25 Gm /100 cc †
Potassium permanganate $KMnO_4$	9 Gm /100 Gm water *	Decomposes †	
Sodium chloride $NaCl$	36 Gm /100 Gm water *	0.4 Gm /100 Gm alc †	Glycerine 10 Gm /100 cc †
Magnesium sulfate $MgSO_4 \cdot 7H_2O$	81.4 Gm /100 Gm water *	1.1 Gm /100 Gm abs alc §	Glycerine 91 Gm /100 cc †
Aluminum chloride $AlCl_3$	69.87 Gm /100 cc water §		Glycerine soluble †
Calcium hydroxide $Ca(OH)_2$	0.15 Gm /100 Gm water *		Glycerine 0.55 Gm /100 cc 20% sol †
Sodium perborate $NaBO_3 \cdot H_2O$	3.78 Gm /100 cc water §		
Zinc oxide $ZnO$	0.001 Gm /100 Gm water §	Insoluble §	
Salticyle acid	0.25 Gm /100 Gm sol †	3.2 Gm /100 Gm sol †	Liquid paraffin nil † Castor oil 11.81 Gm /100 Gm † Olive oil 2.43 Gm /100 Gm †
Benzoic acid	0.345 Gm /100 cc sol †	.47 Gm /100 cc alk §	Castor oil 14.7 Gm /100 Gm † Olive oil 3.96 Gm /100 Gm † Glycerine 9.07 Gm /100 Gm †
Sulfur	Insoluble §	0.003 Gm /100 Gm abs alk †	Wool fat 0.38 Gm /100 Gm † Olive oil 1 Gm /100 cc † Light oil 0.324 Gm /100 Gm sol † Heptane 0.362 Gm /100 Gm sol † Various coal tar oils from 3 to 8.5 Gm /100 cc † Saturated solution calcium hydroxide 0.112 Gm /100 cc †
Phenol	8.8 Gm /100 Gm sol †	Infinitely soluble §	Paraffin 1.66 Gm /100 Gm † Petrolatum soluble † Liquid petrolatum soluble † Glycerine soluble †

\* International Critical Tables, National Research Council, ed 1, New York, McGraw Hill Book Company, Inc., 1926-1930

† Seiden, A. Solubilities of Inorganic and Organic Compounds, ed 3, New York, Van Nostrand Company, Inc., 1940, pt 1, 1941, pt 2

‡ Wood, H. C., and Osol, A. United States Dispensatory, ed 23, Philadelphia, J. B. Lippincott Company, 1943

§ Hodgman, C. D. Handbook of Chemistry and Physics, ed 27, Cleveland, Chemical Rubber Publishing Company, 1943-1944

*B Heat of Vaporization* When a liquid stands in an open container, some of the molecules of that liquid continuously escape from the liquid into the air. The rate of escape of these molecules into the air increases as the temperature is increased until the boiling point is reached. At any temperature less than either boiling point of two liquids, the liquid of the lower boiling point will volatilize at a faster rate than the liquid with the higher boiling point. This rate of evaporation is directly proportional to a property of the liquid called its vapor pressure, i. e., the higher the vapor pressure of a liquid, the more rapid will be its rate of evaporation.

If during the spontaneous evaporation of a liquid in an open container at a temperature below its boiling point the temperature of the liquid is taken at regular intervals, it will be found to decrease. During the process of evaporation heat will be absorbed from the container, and the temperature of the container will drop. This is the situation which exists when a liquid evaporates from the surface of the skin, the

TABLE 2—*Cooling Effect of Various Vehicles*

Vehicle	(A) Vapor Pressure (Cm. of Mercury) 30 C	(B) Molar Heat of Vaporization (Cal./G Mol. Wt.) 30 C	(A × B)	Approximate Relative Cooling Effect
Water	3.15	10,423	32,732	1.0
Ethyl alcohol	7.85	9,808	76,992	2.3
Acetone	28.10	7,547	212,070	6.5
Ether	63.48	6,312	400,686	12.2

temperature of the skin tends to drop and actually does drop unless heat is being supplied to the skin from the underlying tissues or from the surrounding environment at a rate equal to or exceeding the rate at which it is being lost as a result of evaporation and radiation from the surface. The amount of heat lost from the container (supplied to the liquid) when a molecular weight of a liquid evaporates is a property of the liquid and is called its molar heat of vaporization. The larger the molar heat of vaporization the greater the heat loss from the container when the liquid evaporates.

It is thus apparent that the cooling effect on the skin during the evaporation of a liquid will be dependent on the vapor pressure and the molar heat of vaporization of the liquid. Roughly the cooling effect will be proportional to the product of these two factors. Table 2 shows the vapor pressure and molar heat of vaporization of some of the liquids sometimes placed on the skin and the approximate cooling effect of the liquids taking the evaporation of water in dry air as unity.

Such substances as petrolatum also evaporate, but their vapor pressures are so low and their rates of evaporation consequently so slow

that they do not withdraw heat from the skin at a faster rate than it is supplied and therefore do not cool the skin. On the contrary, since they form a relatively occlusive film over the skin, they actually inhibit evaporation of the water normally given off by the skin and therefore have a "heating" effect on the skin.

*C Emulsions and Suspensions*—Vehicles may have a single phase or two phases. A phase is a homogeneous portion of matter which has uniform physical properties and which is separated from other phases by definite bounding surfaces.<sup>3</sup> A phase may be gaseous, liquid or solid, but gaseous phases will be given no consideration here since no vehicle is used in dermatologic therapy in which a gas is one of the phases. The two phase vehicles which are used consist of either two liquid phases (emulsions) or a solid and a liquid phase (suspensions). Petrolatum and the semisolid fats should be thought of as liquids, since at the cutaneous temperatures at which they are used they have the properties of a liquid.

In a two phase system, one substance is dispersed as small particles in the second substance. The substance existing as distinct small particles is called the "dispersed" or "internal" phase; the second substance constitutes the "continuous" or "external" phase.

If two immiscible liquids such as oil and water are shaken together, one of the substances will be dispersed in the other. Soon after the shaking has stopped, however, the substances will again separate into two layers. Such a dispersion would be of little value as a vehicle. In order to be a satisfactory vehicle, a dispersion must be relatively permanent, i. e., it must show little change in its physical characteristics when it ages, when drugs are added to it or when it is subjected to changes in temperature and  $p_H$  (within limits).

In order to make a relatively permanent emulsion it is usually necessary to add a small quantity of a third substance to the two main constituents of the emulsion—the oil and the water. This third substance is called the emulsifying agent. The detailed theory of the action of emulsifying agents may be found in almost any textbook on physical or colloidal chemistry or in a book specifically covering this subject by Clayton.<sup>4</sup> The theory of emulsification will be discussed here in only brief and general terms.

When two immiscible liquids are stratified, there is a relatively small area of contact between them. When, however, one of these liquids is broken up into very small particles which are uniformly dispersed in

3 Getman, F. H., and Daniels, F. *Outlines of Physical Chemistry*, ed. 7, New York: John Wiley & Sons, Inc., 1943.

4 Clayton, W. *Theory of Emulsions and Their Technical Treatment*, Philadelphia, The Blakiston Company, 1943.

the second liquid, there is a great increase in the surface of contact. This results in a large increase in the surface energy, and the greater the surface energy, the more unstable is the dispersion. Decreasing the size of the particles of the dispersed phase only serves to increase the total surface energy. This surface energy is the product of the area and the surface tension between the two liquids at the surface of contact, i.e., the interfacial tension. An emulsifying agent is a substance which will reduce the interfacial tension and consequently the total surface energy and thus tend to stabilize the emulsion.

The size of the dispersed particles is dependent on the characteristics of the two phases and the emulsifying agent and also on the method used to prepare the emulsion. The diameter of the particles of the dispersed phase is usually from  $10^{-4}$  mm to  $10^{-2}$  mm.

Two immiscible liquids can produce two types of emulsions, either of the liquids can be dispersed in the other. In most emulsions one of the liquids is water and the other is referred to as an oil. The types of emulsions are therefore oil in water and water in oil. In the first case, the oil is the dispersed phase and the water the continuous phase, in the water in oil emulsions, the water is the dispersed phase and the oil the continuous.

The type of emulsion produced is not determined primarily by the relative amounts of the two phases, but is determined by the type of emulsifying agent used. Some substances favor the production of oil in water emulsions, others favor the water in oil type. The important emulsifying agents used in vehicles, grouped according to the type of emulsion which results when they are used, are as follows. Emulsifying agents which favor the production of oil in water emulsions are (1) sodium, potassium and ammonium soaps, (2) sulfated oils, alcohols, esters, etc., (3) mixtures of triethanolamine and fatty acids, (4) gums, such as acacia and tragacanth, (5) alkyl aromatic sulfonates, and (6) polyethers and polyalcohols.

Emulsifying agents which favor the production of water in oil emulsions are (1) sterols and sterol esters, such as wool fat, (2) calcium, zinc and aluminum soaps, and (3) fatty amides, secondary amides and alkylolamides.

Each of these emulsifying agents is characterized by the fact that a portion of its molecule is attracted to water (hydrophilic or polar group) and another part is attracted to the oil (lipophilic, hydrophobic or nonpolar group). The important hydrophilic groups are  $-\text{COOH}$ ,  $-\text{COONa}$ ,  $-\text{SO}_3\text{Na}$ ,  $-\text{OSO}_3\text{Na}$ . The lipophilic group is usually a long chain hydrocarbon.

One may wish to determine whether a certain vehicle is an emulsion and if so what type it is. This is not always easy to do but some of the simpler tests will be given. When the refractive indexes of its



two phases differ, as is usually the case, an emulsion is likely to be more opaque than either of its phases (compare cold cream and mineral oil). A relatively clear material may be an emulsion, but if so it will show a Tyndall effect (scattering a beam of light by the dispersed particles of the emulsion). Once it is determined that the vehicle is an emulsion, its type can usually be determined by one or more of three simple tests

- 1 If a water-soluble dye dissolves easily in the emulsion without agitation, the emulsion is the oil in water type, if an oil-soluble dye dissolves easily, it is the water in oil type

- 2 If an emulsion is easily diluted with water without changing the characteristics of the emulsion, it is an oil in water emulsion, if it dilutes with oil, it is water in oil

- 3 If it is a good conductor of electricity, it is an oil in water emulsion

It has been stated that it is important that an emulsion which is to serve as a vehicle remain stable. And yet in the case of most emulsions, there is a tendency for the particles of the dispersed phase to coalesce, thus tending to cause the emulsion to separate into two layers (creaming or breaking). Certain factors tend to accelerate the rate at which emulsions break, and unfortunately the addition of certain drugs causes many emulsion type vehicles to break. Some of the classes of substances which cause emulsions to break are (1) those substances which appreciably change the  $p_H$  of an emulsion, (2) soluble inorganic salts of polyvalent ions and (3) powders. Some apparently stable emulsions, which might be expected to be good vehicles, break so easily on the addition of certain drugs that they are unsatisfactory vehicles.

If the dispersed phase is a solid and the continuous phase is a liquid, the resultant two phase system is called a suspension. Shake lotions and pastes are examples of such two phase systems. In the commonly used vehicles, the particles of the solid phase are relatively large, and the resultant suspensions are unstable. The solid phase quickly settles when the continuous phase is a liquid of low viscosity, such as water. When the continuous phase is a semisolid material of high viscosity, such as the petrolatum of a paste, the solid phase remains suspended for some time.

In a suspension in which the solid particles are small enough to be colloidal (from 1 to 100 millimicrons), the suspension is relatively stable. When the continuous phase is water, the dispersed phase may be either hydrophobic or hydrophilic. Only the latter type of colloidal suspensions will be discussed here. In this group belong starch, gums and the recently developed colloidal clays or bentonites.

Mixtures of these materials with water vary widely in their physical characteristics. They may be similar to water, such as a starch bath,

or they may have a semisolid consistency, such as a bentonite gel. The characteristics of these suspensions are dependent on such factors as the concentration of the dispersed phase, the method of preparation and the temperature of the suspension.

Many of the hydrophilic colloid preparations are liquid at elevated temperatures (sols) and have a semisolid consistency at lower temperatures (gels). This phenomenon is often experienced in solutions of agar, gelatin or gum. Some of the gels of the hydrophilic colloids so resemble petrolatum that a physician is apt to use them as petrolatum would be used. It should not be forgotten, however, that a large part of the volume of these gels is water and that, therefore, these gels more closely resemble the shake lotions than they do the ointments or pastes so far as their use in dermatologic therapy is concerned.

In smaller amounts, the hydrophilic colloids serve as emulsifying and suspending agents. The gums were included in the foregoing list of emulsifying agents and were seen to favor the production of oil in water emulsions. Colloidal clays have been found to serve as emulsifying agents for both types of emulsions. The addition of a little bentonite to a suspension of zinc oxide causes the particles to stay suspended for a much longer time.

The physical state of the vehicle, that is true solution, emulsion or suspension, will be shown to have an important bearing on the functions of vehicles used in dermatologic therapy.

*D. Theory of Wetting Action.* Few fields of physical chemistry have developed as rapidly during the past two decades as that pertaining to the wetting or surface-active agents. Only recently have these substances been used by the medical profession, and Duemling<sup>5</sup> made the first comprehensive report known to us of their use in vehicles for dermatologic topical therapy. Many of the recently prepared emulsion type ointment bases contain wetting agents as emulsifiers. In many respects, the wetting agents resemble the new detergents which have been discussed by us.<sup>6</sup>

When a liquid or semisolid substance is placed on the skin, a new junction (more correctly called "interface") is formed, i. e., the skin-air interface is replaced by a skin-liquid interface. This phenomenon of a liquid coming into contact with a solid to form a solid-liquid interface is termed "wetting" and those substances which, when added to

<sup>5</sup> Duemling W. W. Wetting Agents. New Synthetic Chemicals of Use in Finer and More Efficient Topical Dermatologic Therapy, Arch. Dermat. & Syph. **43** 264-280 (Feb.) 1941.

<sup>6</sup> Lane C. G., and Blank I. H. Cutaneous Detergents Other Than Soap. in A Symposium on Medical Uses of Soap. Philadelphia J. B. Lippincott Company, 1945.

the liquid, and in establishing this contact are called "wetting agents" or "surface-active agents" Wetting agents may also, of course, aid in establishing contact between two immiscible liquids, in which case the wetting agents are as a rule good emulsifying agents, which have already been discussed Many papers have been published on the physical chemistry of wetting Those interested in the detailed physico-chemical aspects of this subject should consult a series of papers by Bartell and his co-workers<sup>7</sup> and the accompanying bibliographies

Three types of wetting are possible adhesional, spreading and immersional For a consideration of the contact of various vehicles with the skin, only spreading wetting is important Immersional wetting is important, however, in the incorporation of some medicaments into vehicles, particularly the solids into the liquid vehicles

Whether or not a liquid will tend to spread over a solid surface is dependent on the free surface energies involved When a liquid spreads, a solid-air interface is replaced by a solid-liquid interface and a liquid-air interface If the sum of the free surface energies of these two new interfaces is less than the free surface energy of the original solid-air interface, then the liquid will tend to spread, if it is greater, the liquid will not spread Up to now there has been no method devised for measuring these free surface energies, since the interfacial tension cannot be measured when one of the surfaces is a solid The interfacial tension is, however, a function of the contact angle which the liquid makes with the solid The contact angle is the angle between the surface and the tangent to the liquid surface at the point of contact with the solid, measured through the liquid Various methods have been devised for measuring the contact angle The smaller the contact angle, the more easily a liquid spreads over a solid surface Spontaneous, complete spreading takes place only when the contact angle is zero Numerous difficulties arise when an attempt is made to measure the contact angle between a liquid and an uneven, nonhomogeneous surface, such as the cutaneous surface To our knowledge, such a measurement has not yet been successfully made

The ability of a vehicle to wet the skin plays an important role in the action of the vehicle on the skin, and this characteristic will be further considered in the discussion of various functions of the vehicle

<sup>7</sup> Bartell, F E *Wetting of Solids by Liquids*, in Alexander, J *Colloid Chemistry*, New York, Chemical Catalogue Company, 1931, vol 3, pp 41-60 Bartell, F E, and Wooley, A D *Solid-Liquid-Air Contact Angles and Their Dependence upon the Surface Conditions of the Solid*, *J Am Chem Soc* **55** 3518-3527 (Sept) 1933 Bartell, F E, and Bartell, L S *Quantitative Correlation of Interfacial Free Surface Energies*, *ibid* **56** 2205-2210 (Sept) 1934 Bartell, F E *Wetting Agents*, *Indust & Engin Chem* **33** 737-740 (June) 1941

## IV FUNCTIONS OF VEHICLES

A vehicle has many functions to perform. The more important of these functions are as follows:

- A It carries a drug to the skin and holds it there
  - B It influences the penetration of a drug into and through the skin
  - C It alters evaporation from the cutaneous surface
  - D It alters the texture of the skin
  - E It protects the skin
  - F It aids in the removal of cutaneous secretions
- Each of these functions will be discussed for the various classes of vehicles.

*A Carrier for a Drug* This function is probably the most important function of the vehicle. Seldom are drugs applied directly to the skin. They are first dispersed in the vehicle, and it is the function of the vehicle to distribute the drug over the diseased surface of the skin and to hold it there to produce the desired effect. In choosing the vehicle to perform this function, it is necessary to consider three physicochemical characteristics of the vehicle, which are (1) the solvent action of the vehicle for the drug, (2) the volatility of the vehicle and (3) the ability of the vehicle to permit transfer of the drug from the vehicle to the skin.

1 *Solubility of the Drug in the Vehicle* A vehicle may carry a drug in solution or in suspension. When the drug is present in true solution, its state of subdivision is molecular or smaller than molecular. In colloidal solutions of drugs, the particle size is very small but it is larger than molecular. In suspensions, the particle size of the drug is still larger, and its size will be determined by the method used to produce the suspension. The most uniform distribution of the drug over the surface of the skin is accomplished when the drug is in true solution in the vehicle.

In true solutions and in colloidal solutions the drug moves about freely in the vehicle. If the drug is present in suspension, the particles are too large to move and remain in a fixed position. Theoretically, therefore, when a drug is applied to the skin in a vehicle in which it is soluble, the entire amount of the drug is available to the skin. That is to say, those molecules of the drug which are not at the interface between the vehicle and the skin when the therapeutic material is first applied to the skin will reach the interface at some later time because they move about freely in the solution. When the drug is present in suspension, however, only those particles of the drug which are at the interface when the material is applied will come into contact with the skin. The particles at a distance from the interface cannot move about and are not available to the skin. It would be expected, therefore, that

when salicylic acid is applied to the skin in castor oil, in which it is soluble, much more of the salicylic acid would be available to the skin than when it is applied in petrolatum, in which it is insoluble

When the concentration of a drug which is soluble in a given vehicle is increased within the limits of its solubility, it may be theoretically assumed that the action of that drug on the skin will be increased in direct proportion to the increase in concentration. Consider the example in which the concentration of the drug is doubled. The number of molecules of the drug originally in contact with the skin will be doubled, and the number reaching the skin as the molecules move about will likewise be doubled. The action on the skin should therefore also be doubled.

When the concentration of a drug which is insoluble in a given vehicle is increased, the action of the drug on the skin may not be increased in direct proportion to the increase in concentration. When the concentration is doubled, the amount of drug in contact with the skin when first applied will be doubled but if some of this is used up by reaction with the skin, no more will be brought to the surface of the skin, since the suspended particles do not move about in the vehicle. Therefore, a 2 per cent solution of salicylic acid in castor oil might be expected to have twice the effect on the skin of a 1 per cent solution, but it does not follow that a 2 per cent suspension of salicylic acid in petrolatum will have twice the effect of a 1 per cent suspension.

This last example of an insoluble drug in a nonvolatile, oily vehicle represents the type of therapeutic material most commonly used in the treatment of diseases of the skin. Petrolatum is a frequently used vehicle, and most drugs are relatively insoluble in it. In doubling the concentration of a drug in petrolatum, a physician often feels that he has prescribed an ointment which is twice as strong as a previously prescribed ointment. Strakosch<sup>2</sup> showed that the keratolytic action of salicylic acid in petrolatum is increased by increasing the concentration of the salicylic acid, but that the rate of keratolytic action is not increased in direct proportion to the change in concentration of the salicylic acid. Abramowitz<sup>8</sup> found that some ointments containing large amounts of sulfur were apparently milder than ointments containing less sulfur.

**2 Volatility of the Vehicle** When a large volume of a therapeutic material made with a volatile vehicle is used for a short time only, evaporation of the vehicle does not alter the action of the therapeutic material on the skin. The small amount of evaporation which takes place when an extremity is soaked for a short time in a large volume

<sup>8</sup> Abramowitz, E. W. External Use of 30 to 50 Per Cent Sulfur in Petrolatum in Various Dermatoses, *New York State J. Med.* **43** 746-753 (April 15) 1943

of boric acid solution or when a potassium permanganate bath is taken changes the action of these solutions little because the concentration of the drug is only slightly increased. When only a small volume of such a therapeutic material is used, however, the evaporation of the vehicle may definitely alter the action of the material on the skin.

The entire vehicle may be volatile, such as ethyl alcohol, or only part of the vehicle may be volatile, such as emulsions or collodions. When the entire vehicle is volatile, the drug which it contains will be deposited on the skin "in 100 per cent concentration" after the vehicle evaporates, independent of the original concentration of the drug in the therapeutic material. When the vehicle is as volatile as alcohol, the concentration rapidly changes after the therapeutic material is applied to the skin. Stronger tincture of iodine (7 per cent) will deposit three and one-half times as much iodine on the skin as will mild tincture of iodine (2 per cent) when equal volumes of the two solutions are placed on equal areas of the skin. Any greater reaction which may result from the application of stronger tincture of iodine will be caused not by the action of the 7 per cent iodine solution as such but by the greater amount of iodine deposited on the skin when the vehicle evaporates.

When a vehicle a portion of which is easily volatile is prescribed, it must be remembered that the characteristics of the therapeutic material and the concentration of the drug as specified by the physician are changed subsequent to the evaporation of the volatile part of the vehicle. When an oil in water emulsion, such as a vanishing cream, is used as a vehicle, the water phase quickly evaporates, leaving a film of a water-miscible oil with the drug probably in suspension. The original advantage of having the drug in solution (if the drug is water soluble) disappears when the water evaporates. Likewise when a vehicle is a shake lotion or a gel of a hydrophilic colloid, the evaporation of the water leaves the drug on the skin mechanically mixed with a hydrophobic or hydrophilic powder (for the shake lotion) and with a hydrophilic film (for the colloidal gel). In the case of collodions, a large percentage of the drug may be made inactive when it is encased in a hydrophobic film after the evaporation of the solvent.

3 Transfer of the Drug from the Vehicle to the Skin. Before a drug can exert a true chemical or physiologic action on the skin, it must be transferred from the vehicle which has served as its carrier to the skin itself. Also, chemical and physiologic reactions in the skin probably take place in an aqueous environment. Therefore, if a drug should be transferred from the vehicle to the oily film of the skin, such as the sebum, it must be further transferred to an aqueous fluid, such as perspiration or serous exudate. The skin, of course, contains large amounts of water and is continually giving off water as insensible and

sensible perspiration, which may accumulate on the cutaneous surface or in the cutaneous tissue if normal evaporation is inhibited by the vehicle. In some cutaneous lesions the surface is wet by serous exudate in other lesions and in normal skin, oily sebaceous secretions probably constitute the surface film. The transfer of the drug from the vehicle to the skin will depend on the miscibility of the vehicle with the substances on the cutaneous surface and on the relative solubility of the drug in the vehicle and the cutaneous fluids.

A vehicle will be completely miscible only with a skin secretion or exudate which has characteristics similar to those of the vehicle. For instance, an aqueous vehicle will mix easily and completely with a serous exudate or with sweat but will not mix easily with an oily secretion such as the fatty film on the surface of normal unbroken skin. A hydrophobic oily vehicle, such as petrolatum, on the other hand, will mix with the fatty film but will not mix with sweat or with a serous exudate. A hydrophilic oily vehicle, such as wool fat, may be able to mix with both oily and aqueous surface films. Drugs in solution in aqueous vehicles will be easily transferred to aqueous cutaneous secretions or exudates, drugs which are readily soluble in oily vehicles will be easily transferred to oily cutaneous secretions.

The transfer of a drug dissolved in a vehicle to a cutaneous fluid with which the vehicle is not miscible may occur and will depend on the relative solubility of the drug in the vehicle and in the cutaneous fluid. A solute will distribute itself between two immiscible solvents in direct proportion to its relative solubility in the two solvents. Salicylic acid is six times more soluble in castor oil than in olive oil. Since it is much more soluble in either oil than in water, however, the amount of salicylic acid which will be transferred to water (and probably to aqueous cutaneous fluids) from a saturated castor oil solution will be little more than the amount that will be transferred from a saturated olive oil solution. The total reserve salicylic acid will, of course, be much greater in the castor oil solution.

A drug suspended in a vehicle may be dissolved out of the vehicle by a cutaneous fluid or secretion. This would be a type of leaching process. That is to say, salicylic acid may be leached from petrolatum in which it is suspended, by the aqueous cutaneous fluids, if these fluids can get in contact with the salicylic acid crystals. Probably, however, these crystals are coated with a film of petrolatum, and it is therefore difficult for water to come in contact with the crystals. The mechanism by which a salicylic acid crystal completely coated with petrolatum can become available to the aqueous fluids of the skin is not apparent to us. Possibly the salicylic acid is transferred to the more hydrophilic sebum from the petrolatum and can then be transferred to the aqueous fluids.

4 Summary (a) When a vehicle carries a drug in true solution the drug will be distributed more uniformly over the surface of the skin than when the vehicle carries the drug in suspension

(b) The action of a drug on the skin is more likely to vary in direct proportion to its concentration if a vehicle is used in which the drug is soluble than if one is used in which the drug is insoluble

(c) When a volatile vehicle evaporates, the concentration of the drug changes and the means by which the drug is held on the skin is altered

(d) A drug will be transferred most easily to the skin if the vehicle in which it is dissolved is similar to the cutaneous secretion or exudate with which it comes in contact

(e) Transfer of a drug from a vehicle to a cutaneous fluid with which the vehicle is not miscible will depend on the relative solubility of the drug in the vehicle and in the cutaneous fluid

*(To Be Continued)*



# DERMATITIS FROM A LARGE DOSE OF PENICILLIN TAKEN ORALLY

Report of a Case

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CINCINNATI

IT IS not infrequent to find sensitivity to penicillin in persons who come in contact with it or who have received it intramuscularly or intravenously. No report has been found in the literature describing this reaction after oral administration. Penicillin is described as a drug having practically no toxicity and of which extremely large doses are tolerated for long periods of time without ill effects.

Lyons<sup>1</sup> reported an urticarial reaction in 12 out of 209 patients receiving penicillin therapy. Pyle and Rattner<sup>2</sup> recorded a case of dermatitis venenata of face and genitalia in a physician who came in contact with penicillin while preparing solutions and administering them to patients. Three of his orderlies handling penicillin also experienced slight itching, though no dermatitis developed. Binkley and Brockmole<sup>3</sup> reported 2 cases of contact dermatitis in which there was a focus of dermatophytosis pedis on the webs of the toes. Barker<sup>4</sup> reported 2 cases in which cutaneous lesions developed after clinical use. Crip<sup>5</sup> discussed a case of acquired sensitivity to penicillin in which he believes the allergy to be unrelated to penicillin spores, but to be analogous to drug or serum allergy. Feinberg<sup>6</sup> stated that the penicillin reaction does not resemble the classical and severe allergic reactions which would be likely to follow the injection of an allergen to which the person

From the Department of Biochemistry, The Wm S Merrell Co (Dr Oberst) and the Department of Physiology, University of Cincinnati (Dr Murray)

1 Lyons, C. Penicillin Therapy of Surgical Infections in the U S Army, J A M A **123** 1007-1018 (Dec 18) 1943

2 Pyle, H D, and Rattner, H. Contact Dermatitis from Penicillin, J A M A **125** 903 (July 29) 1944

3 Binkley, G W, and Brockmole, A. Dermatitis from Penicillin, Arch Dermat & Syph **50** 326-327 (Nov ) 1944

4 Barker, A N. Allergic Reactions to Penicillin, Lancet **1** 177-178, 1945

5 Crip, L H. Allergy to Penicillin, J A M A **126** 429-430 (Oct 14) 1944

6 Feinberg, S M. Penicillin Allergy, J Allergy **15** 271-273, 1944

has been naturally sensitive. He showed that when a fairly pure preparation of penicillin (630 units per milligram or greater) was administered no reaction was obtained in a penicillin-sensitive patient after a dose of at least 500,000 units.

During the course of a study on urinary excretion and blood levels of penicillin after oral and intravenous administration of penicillin,<sup>7</sup> one of us (F W O) who served as a subject reacted severely to 50,000 units given intravenously. Within an hour he showed a dermatitis which after several hours became severe. The face reddened, small areas of erythema appeared all over the chest, and some swelling and small blisters appeared around the toes. The scalp and toes itched considerably at times. This general condition lasted for about three days.

Several weeks later the same dose of penicillin was taken orally with no noticeable reaction appearing. Repeated administrations at biweekly intervals of this size dose with and without food and with and without antacids were made at least ten times without producing a reaction at any time. However, when the dose was increased to approximately 500,000 units, a severe dermatitis resulted similar to the one from the 50,000 unit dose given intravenously. The penicillin used was suspended in oil and beeswax, put in soft gelatin capsules, and had a purity of 842 units per milligram.

About two hours after the oral dose there was itching of the toes, which were severely swollen about ten hours later. Numerous small blisters appeared in the web, followed by some oozing and lesions. By the third day small patches of epidermis peeled off where the lesions occurred. There was also a mild dermatitis on the chest, in the groin and under the chin, with some swelling and reddening around the eyes. The person had no history of eczema and had not previously experienced any allergic reactions. There was no evidence of fungous infection which might render him sensitive to a mold product occurring as an impurity in the product.

The mechanism for this condition is not clear, as other persons taking the same dose did not have dermatitis. It generally is believed that the reaction is not due to the penicillin per se but to impurities associated with it. By giving penicillin orally it was hoped that the chances of producing a dermatitis might be considerably decreased, unless the substance responsible for the reaction is absorbed from the

<sup>7</sup> Oberst, F W, Nielsen, F A, and Foter, M J. Blood Levels and Urinary Excretion of Penicillin After Oral Administration, Cincinnati J Med, October 1946, to be published.

gastrointestinal tract The dose used here was approximately ten times that given intravenously Some authorities<sup>8</sup> state that it requires about five to ten times as much penicillin when given orally as when given intravenously or intramuscularly to obtain the same clinical effect After the oral dose in this case there was undoubtedly about the same effective penicillin concentration in blood and tissues as after the 50,000 unit dose given intravenously

<sup>8</sup> Keefer, C S Status of Oral Penicillin, *J Am Pharm A (Pract Pharm Ed)* **6** 210, 1945

# CONTACT DERMATITIS FROM PENICILLIN

The Source of the Antigen

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DETROIT

AND

ROBERT M WATROUS, M D

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CHICAGO

**A**LLERGY to penicillin has been the subject of many recent reports. Various types of reactions are recorded which may be classified under the heading of hypersensitivity. The most common allergic response described is urticaria<sup>1</sup>. In most instances this resembles a serum sickness type of reaction and does not interfere with the continuation of treatment. In a few cases, more severe reactions have necessitated prompt cessation of therapy. Another type of reaction is a vesicular or bullous eruption occurring shortly after the onset of treatment, which appears to be in some manner related to a previous fungous infection of the skin<sup>2</sup>. Contact dermatitis is a third manifestation of

The materials used in this study were supplied by the Abbott Laboratories, North Chicago, Ill.

From the Division of Allergy, Department of Medicine, Northwestern University School of Medicine, and the Plant Physician's Department of Abbott Laboratories.

1 Keefer, C S, Blake, F G, Marshall, E K, Jr, Lockwood, J S, and Wood, W J Jr, Penicillin in the Treatment of Infections. A Report of Five Hundred Cases, *J A M A* **122** 1217-1224 (Aug 28) 1943. Lyons, C. Penicillin Therapy of Surgical Infections in the U S Army, *ibid* **123** 1007-1018 (Dec 18) 1943. Crippe, L H. Allergy to Penicillin, *ibid* **126** 429-430 (Oct 14) 1944. Price, D E, McNairy, D J, and White, E L. Severe Asthma. Delayed Sensitization to Penicillin, *ibid* **128** 183 (May 19) 1945. Sullens, W E. Simulating Serum Sickness Reaction to Penicillin, *U S Nav M Bull* **45** 752-754 (Oct) 1945.

2 Graves, W N, Carpenter, C C, and Unangst, R W. Recurrent Vesicular Eruptions Appearing During Administration of Penicillin, *Arch Dermat & Syph* **50** 6-7 (July) 1944. Cohen, M T, and Pfaff, R O. Penicillin in Dermatologic Therapy. Report of Results of One Hundred Cases, *ibid* **51** 172-177 (March) 1945. Binkley, G W, and Brockmole, A. Dermatitis from Penicillin. Report of Two Cases, *ibid* **50** 326-327 (Nov) 1944. Morris, G E, and Downing, J G. Bullous Dermatitis (Dermatitis Medicamentosa) from Penicillin, *J A M A* **127** 711 (March 24) 1945. Lamb, J H. Allergic Reactions During the Administration of Penicillin, *Arch Dermat & Syph* **52** 93-95 (Aug) 1945.

quently attributed to penicillin<sup>3</sup> In addition to these three types of allergy, which comprise the majority of the reactions reported, a tuberculin type of response following a single intradermal injection,<sup>4</sup> and reactions of the Arthus type following repeated intradermal injections have been noted<sup>5</sup>

Since the penicillin in common use contains a fair amount of impurities, doubt has arisen that the allergic reactions observed are caused by the active principle of penicillin itself In a recent review of the subject, one of us (S M F)<sup>6</sup> pointed out that the majority of reports lack in some respect the details necessary to provide a complete picture of the source and mechanism of allergy to penicillin It is quite possible that more than one antigen accounts for the varied allergic reactions already noted A more thorough study of patients presenting allergic symptoms from penicillin is necessary to determine the source and mechanism of such reactions

We have recently encountered 5 cases of contact dermatitis in persons handling penicillin All of the patients were completely relieved of symptoms when removed from contact with the drug Four of these patients were industrial workers engaged in the manufacture of penicillin for commercial use, and 1 was a chemist producing the drug by the surface culture method for experimental study We availed ourselves of the opportunity of determining the source of the allergen in these cases by making patch tests with substances entering into the manufacture of penicillin, the commercial penicillin salts and a chemically pure preparation of crystalline penicillin G In addition, intradermal tests were carried out with mold extracts to determine any relationship that might exist between contact dermatitis and clinical allergy to molds Four of the patients were available for testing at the time this study was made

3 (a) Pyle, H D, and Rattner, H Contact Dermatitis from Penicillin, *J A M A* **125** 903 (July 29) 1944 (b) Silvers, S H Contact Dermatitis from Amorphous Sodium Penicillin, *Arch Dermat & Syph* **50** 328-329 (Nov) 1944 (c) Barker, A N Allergic Reactions to Penicillin, *Lancet* **1** 177-178 (Feb 10) 1945 (d) Hanson, P S Contact Dermatitis Caused by Commercial Penicillin A Case Report, *M Bull North African Theat Op* **2** 118 (Nov) 1944 Nelson, L M, and Sandt, K E Contact Dermatitis of the Eyelids as Result of Penicillin, *ibid* **2** 62 (Sept) 1944 Michie, W, and Bailie, H W C A Case of Penicillin Reaction, *Brit M J* **1** 554 (April 21) 1945 Selinger, E Dermatitis of the Lids from Penicillin Eye Drops, *J A M A* **128** 437 (June 9) 1945

4 Welch, H, and Rostenberg, A, Jr Hypersensitivity of Tuberculin Type to Crystalline Penicillin Sodium, *J A M A* **126** 10-12 (Sept 2) 1944

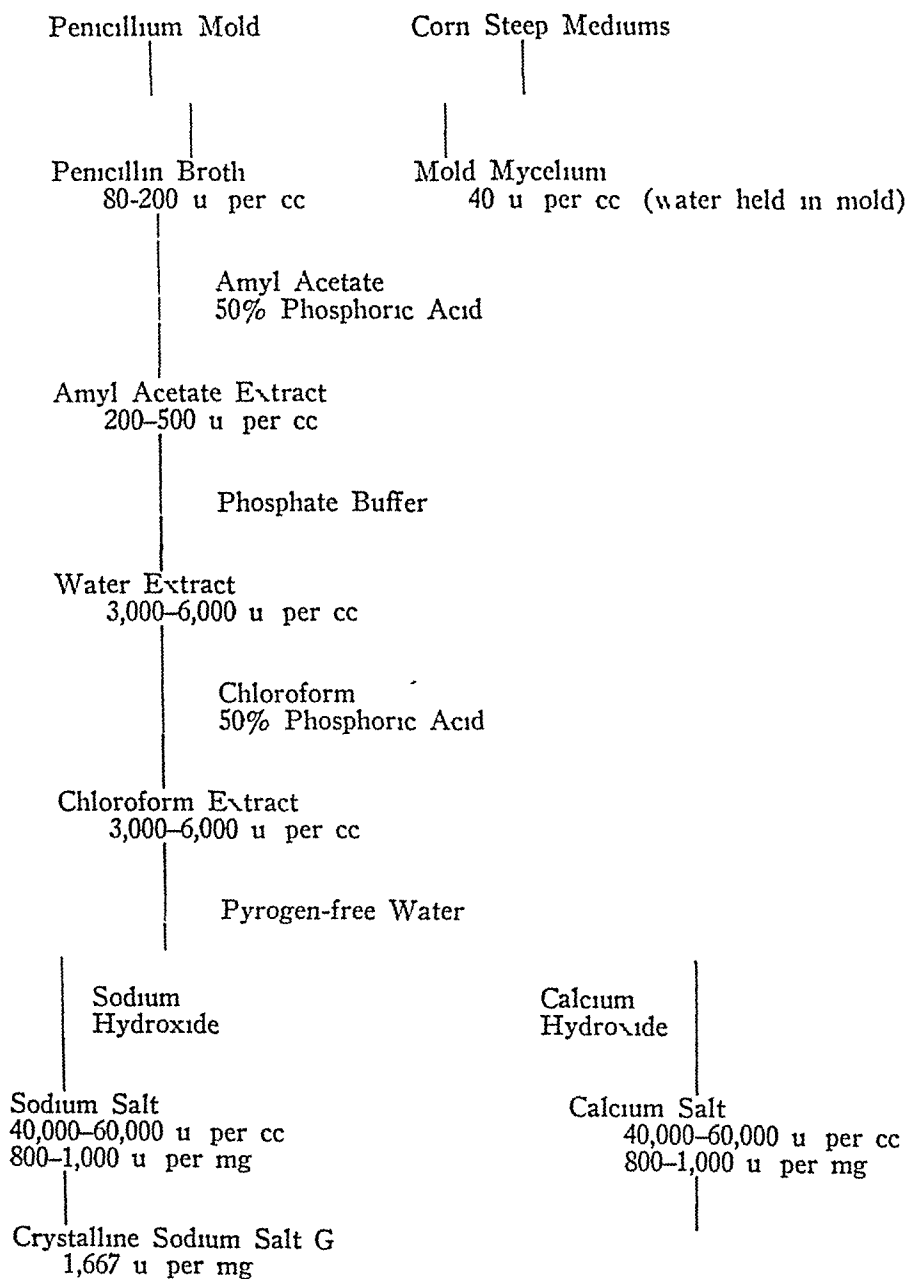
5 Rostenberg, A, Jr Local Penicillin Therapy, *Arch Dermat & Syph* **50** 330 (Nov) 1944

6 Feinberg, S M Allergy to Penicillin, *J Allergy* **16** 302 (Nov) 1945

# PRODUCTION OF PENICILLIN<sup>7</sup>

Most commercial preparations of penicillin are produced by the submerged broth method. A strain of *Penicillium chrysogenum* is grown in a corn steep liquor containing lactose and mineral salts. After adequate growth the mold mycelium is separated from the broth and extracted with solvents, such as amyl acetate and chloroform, finally ending up as the sodium or calcium salt of penicillin.

## *The Production of Penicillin*



<sup>7</sup> Sylvester, J. C. Personal communication to the author.

The final solution is lyophilized to produce a powder containing approximately 60 to 70 per cent of penicillin. Approximately 90 per cent of the sodium or calcium salt is penicillin G. The crystalline sodium salt G is produced from commercial penicillin and is chemically pure (diagram). The surface culture method is not as well adapted for quantity production. A strain of *Penicillium notatum* is generally used, and the penicillin obtained contains appreciable amounts of penicillin X in addition to penicillin G.

#### REPORT OF CASES

CASE 1—V J, a 30 year old married woman, was employed in the penicillin department on May 26, 1944. Her work consisted of placing muslin covers over aluminum trays containing penicillin which had previously been frozen and dried to form a powder. On March 3, 1945 a pruritic eruption developed on the dorsum of the left hand and on the right wrist. A boric acid cream was prescribed, and the eruption improved for a time but recurred later. On two occasions she was away from work for periods of ten days and noted a decided improvement of the eruption, with recurrence on her return to work. On May 2, 1945 the eruption became aggravated, and in addition itching of the neck and eyelids developed. The patient was then transferred to another department, where all contact with penicillin was avoided. The dermatitis gradually cleared and has not recurred.

CASE 2—J M, a 56 year old man, was employed in the penicillin department on Jan 12, 1944 and engaged in the extraction processes. On March 9, 1945 a pruritic eruption developed on the dorsa of the hands and forearms, with a diffuse maculopapular eruption on the face, forehead and neck. Local therapy failed to produce improvement. He was then removed from the penicillin division, and rapid disappearance of the eruption was observed without subsequent recurrence.

CASE 3—J R, a 33 year old man, was employed in the penicillin department on Oct 14, 1943. His work consisted of the final extraction and purification of penicillin. Approximately four months later a pruritic vesicular eruption developed on the lateral and dorsal aspects of both hands. Hydrous wool fat and ointment of benzoic and salicylic acid were applied without relief. The wearing of cotton and rubber gloves failed to cause any improvement. He was seen on Oct 24, 1945 with a vesicular scaly eruption on the fingers and hands and a diffuse eruption on the flexor surface of the right forearm. A sulfonated oil was prescribed, and soap and water were avoided for a period. As there was no improvement he was transferred from the penicillin department, after which the eruption disappeared.

CASE 4—H L, a white married woman, 52 years of age was employed in the penicillin department on Jan 5, 1944. Her work consisted of inoculating the corn steep liquor with a suspension of *Penicillium* mold. Some time before November a dermatitis developed on the dorsal aspects of the hands and fingers. This was treated with cod liver oil and boric acid ointments, without improvement. She continued to work in the penicillin department until March 9, 1945, when an exacerbation of the dermatitis occurred on the forearms and face, as well as on the hands. She was then removed from her job, and the eruption was completely gone by March 23.

CASE 5—C F, a chemist aged 58, began producing penicillin by the surface culture method in September 1943. On March 3, 1945 a burning and itching of the eyelids developed and an eczematoid weeping eruption appeared on the skin of the

orbital regions. He discontinued work and was given several roentgen ray treatments to the involved areas, with gradual disappearance of the eruption. On April 8 he had a slight sore throat, and as a prophylactic measure he sprayed his throat with a penicillin solution containing 8,000 units per cubic centimeter. Shortly afterward he again noted itching of the eyelids with subsequent reappearance of the eruption, as well as itching and edema of the soft palate, uvula, and pharynx. Avoidance of penicillin resulted in prompt disappearance of symptoms. Later he tried taking penicillin in the form of a lozenge by mouth. This was followed in a few moments by itching and inflammation of the pharynx.

### TESTING AND RESULTS

Individual patch tests were made on the back or on the lateral aspect of the arm. To insure potency, the substances used were obtained from a routine production run a few moments before their application. The patches were removed and the reactions noted at forty-eight hours, and a final reading was made at seventy-two hours.

#### *Results of Test*

	V J	J M	J R	C F
Penicillium mold	0	0	0	+
Corn steep liquor mediums	0	0	0	0
Mold mycelium (submerged culture) water held in mold containing 40 u/cc	++	++	+	
Mold pellicle (surface culture)				+
Penicillin broth, 200 u/cc	++	0	0	+
Amyl acetate extract, 300 u/cc	+	0	0	
Water extract, 5,000 u/cc	+++	+	0	
Chloroform extract, 3,000 u/cc	++	+	+++	
Sodium salt of penicillin, 50,000 u/cc	++	+	0	++
Calcium salt of penicillin, 50,000 u/cc	++	+	0	
Crystalline sodium penicillin G, 8,000 u/cc	+++	+	0	+++
Penicillium notatum 1:1,000 (intracutaneously), alternaria 1:1,000	0	0	0	0

+, slight, ++, moderate, +++, strong

Intradermal tests with mold extracts were made on the forearm. Readings were made at fifteen minutes and at forty-eight and seventy-two hours. The results are summarized in the table.

Reactions to pure crystalline penicillin as well as to intermediary products were noted in 3 of the cases studied. These were significant in that tests on control subjects elicited negative reactions. In 1 patient (C F) a reaction occurred to the *Penicillium* mold, indicating that at least a small amount of the active principle of penicillin is contained in the original mold itself. Another patient (J R) failed to show reactions to the crystalline or the commercial preparations. A strong reaction to the chloroform extract was obtained, and a lesser reaction to the mold mycelium containing relatively little penicillin. At an earlier date, this subject was reported to have given a positive reaction to a patch test with dry penicillin powder containing 1,000 units per milligram. It is likely that the dermatitis observed in this patient was due to substances other than penicillin. Control tests with the mold mycelium



elicited negative reactions. The corn steep liquor medium failed to cause a reaction in any subject. No reactions, either immediate or delayed, occurred to the intradermal injections of mold extracts.

#### COMMENT

The rapidly increasing use of penicillin locally in such forms as ointments, sprays, drops, troches and lozenges will create many opportunities favoring the development of the contact type of allergic reaction. It is therefore of importance to recognize the potentialities of penicillin as a skin-sensitizing agent and to determine the active principle responsible for such reactions. Some attempt to locate the responsible factor has been made in previous reports. Pyle and Ratner<sup>3a</sup> described a case of contact dermatitis. The patient was a physician handling penicillin in whom patch tests with the commercial preparation and with the purest crystalline material then available elicited positive reactions. Silvers,<sup>3b</sup> on the other hand, reported an instance of dermatitis in a chemist working with penicillin who had a strong reaction to yellow amorphous penicillin but a negative one to the crystalline preparation. In a case reported by Barker<sup>3c</sup> the patient had a positive reaction to a patch test with the commercial penicillin, but a similar solution previously autoclaved failed to elicit a reaction. In the present study, the patients presented eczematoid eruptions localized to the areas of maximum exposure. Removal of the offending agent resulted in prompt recovery, and subsequent exposure in certain instances reproduced the dermatitis. In 3 patients, sensitivity to the active principle of penicillin rather than to the impurities contained in the commercial product was definitely determined.

The development of contact dermatitis to any agent depends on the potency of the allergen, the length of contact and the condition of the skin, rather than to any constitutional or preformed systemic condition.<sup>8</sup> The absence of personal or familial histories of allergy in the present series and negative cutaneous reactions to the *Penicillium* and *Alternaria* molds indicate that little connection exists between contact dermatitis to penicillin and clinical allergy to mold. That penicillin contains little if any of the antigen residing in the *Penicillium* fungus has already been determined.<sup>9</sup>

The patients in this study as well as the majority of those described in the literature have been persons engaged in the manufacture or in the handling of penicillin, rather than patients under treatment with

8. Feinberg, S. M. *Allergy in Practice*, Chicago, The Year Book Publishers, Inc., 1944.

9. Feinberg, S. M. *Penicillin Allergy: On the Probability of Allergic Reactions in Fungus Sensitive Individuals, Preliminary Experiments*, *J. Allergy* **15** 271-273 (July) 1944.

the drug. This is readily understood when it is recalled that until recently penicillin was employed chiefly by the parenteral route. No prolonged and repeated contact with the skin or mucous membrane had occurred in the vast majority of patients treated. In our present series we noted that a relatively long period of contact with the allergen (nine to eighteen months) was necessary before sensitization became manifest. It is also conceivable that the skins of persons handling chemicals possess a lower tolerance to allergenic agents than the skin of the average person.

It is not yet entirely clear how potent an allergen penicillin is. McCloskey and Smith<sup>10</sup> were able to produce anaphylactic sensitization to commercial penicillin in guinea pigs. Rostenberg<sup>6</sup> found that repeated injections of penicillin caused an Arthus type of response in the majority of human subjects. In a study of 27 patients receiving prolonged and intensive parenteral treatment, Grolnick and Loewe<sup>11</sup> failed to find any in whom there developed sensitivity to penicillin or to the notatum mold. That penicillin may not be an exceedingly strong allergen is also suggested by the relatively few cases of allergy already encountered in clinical practice and, in the case of dermatitis, by the long period of contact necessary before sensitivity ensues. It is likely, however, that in the employment of penicillin in local therapy there will arise many instances in which such prolonged and repeated contact will be desirable or necessary. In such cases the physician must bear in mind the fact that penicillin is capable of producing an allergic dermatitis of the contact type.

#### SUMMARY

Contact dermatitis was encountered in 5 persons handling penicillin. A study was carried out in 4 of the cases to determine whether the source of the sensitizing agent was penicillin or the impurities contained in the commercial preparation.

In 3 cases a sensitivity to the active principle of penicillin was definitely determined. No relationship between contact dermatitis due to penicillin and clinical allergy to molds was observed.

Prolonged and repeated contact with penicillin was noted before dermatitis ensued. It is pointed out that similar conditions favorable to the development of contact dermatitis will occur in many patients receiving topical penicillin therapy.

10 McCloskey, W. T., and Smith, M. I. Experiments on the Sensitizing Properties of Penicillin, *Proc Soc Exper Biol & Med* **57** 270-275 (Nov) 1944.

11 Grolnick, M., and Loewe, L. Immunologic Studies in Patients with Subacute Bacterial Endocarditis Treated by Combined Penicillin-Heparin Method. I. Sensitivity to Penicillin, *J Lab & Clin Med* **30** 559-563 (July) 1945.

## OBSERVATIONS ON THE CAUSE AND TRANSMISSION OF GRANULOMA INGUINALE

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AND

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IN 1937 studies on 8 cases of granuloma inguinale were reported by one of us<sup>1</sup>. In that report it was suggested that a spirochete and a short stout coccobacillary rod might be etiologically related to the disease. It was also suggested in the same report that the disease might be transmitted by means of the pubic louse, *Phthirus pubis* (Linn.)

It was not until 1943 that studies were resumed along these lines. In the present series all the patients were Negroes, and, with but 1 exception (case 9), all were admitted to Gallinger Municipal Hospital for diagnosis and treatment.

Three pertinent observations appear to have been demonstrated or suggested by this report.

The first observation is that in 10 of the 11 cases (91 per cent) in which the pathognomonic leishmania bodies were found in biopsy material a history of infestation with *P. pubis* preceding the appearance of the initial lesion was obtained (table). In 3 cases observed by one of us (D B) in 1943, in Trinidad, British West Indies, a similar history was obtained. We do not wish to stress the observation that in the 4 cases of this series in which no leishmania bodies could be found the patients gave no history of pubic pediculosis. However, we do wish to emphasize the fact that pubic pediculosis is not rare among Negroes, a fact contrary to common opinion. In this connection it is interesting to note that in 6 of the 11 cases (54 per cent) in which leishmania bodies could be found the initial lesion was extra-genital, having appeared in areas frequently infested by *P. pubis* (pubic and perianal).

A table which accompanied this article has been lost. If it is found, it will be incorporated in the authors' reprints.

From the Department of Bacteriology and Preventive Medicine, Georgetown University School of Medicine (Dr Butts), and the Rapid Treatment Center, Gallinger Municipal Hospital (Dr Olansky).

1 Butts, D C A. *Am J Syph, Gonorr & Ven Dis* 21: 544-553, 1937.

The second interesting observation is that in no case in which the patient was married was there a history of the wife's being affected, although several of the patients had suffered from the disease for a period of years (table) The same observation was previously reported by one of us<sup>1</sup>

The last and most significant observation is one which we feel supports the work recently reported by Anderson, DeMonbreun and Goodpasture<sup>2</sup> and which was suggested by one of us (D B ) before



Fig 1 (case 9) —A 19 year old single Negro woman had had the disease for about seven weeks Serologic reaction was negative for syphilis Frei and Ducrey tests were negative Vaginal smears were negative for gonococci The biopsy material was removed from the ulcerated area underlying the left labium majus (showing pronounced elephantiasis) Observations recorded in figures 2, 3, 4 and 5 were obtained from this case

the Atlantic Dermatological Conference in February 1944 Rather late in the study of this series of cases (case 9) an attempt to culture

2 Anderson, K , DeMonbreun, W A , and Goodpasture, E W J Exper Med 81 25-39, 1945

the etiologic agent of granuloma inguinale was undertaken. The disease in this case was at an early stage, the biopsy specimen showing numerous leishmania bodies and typical coccobacillary forms of microorganisms but being free of any spiral forms. Serologic tests for syphilis elicited negative reactions. For these reasons it seemed an excellent case for such a study (fig 1).

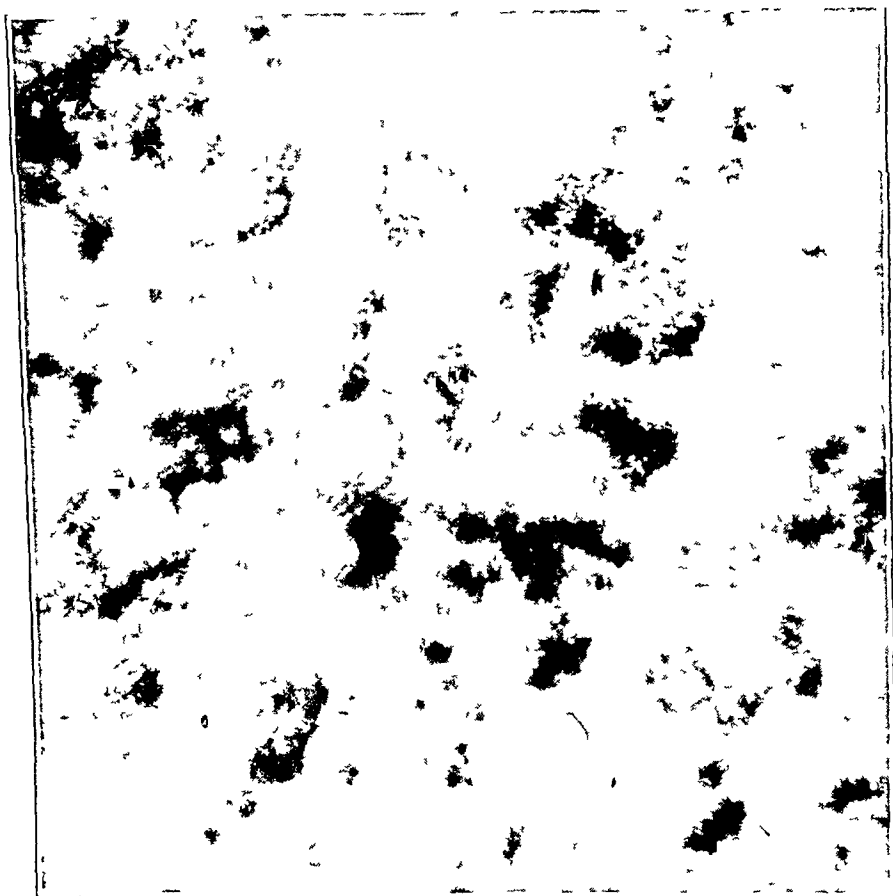


Fig 2 (case 9) —Gram stain slide from a culture (anaerobic) after four days, growth on ascitic agar. Note rings and clusters of bacteria-like bodies scattered throughout the staphylococci.

Tubes of ascitic agar were inoculated with the tissue immediately on removal from the lesion. These were incubated at 37 C under aerobic and anaerobic conditions. For anaerobic cultivation, the modified Rosenthal chromium-sulfuric acid method, as suggested by Mueller and Miller,<sup>3</sup> was employed. After four days of anaerobic incubation, there appeared small translucent colonies near the water of syneresis in the tubes.

3 Mueller, J. H., and Miller, P. A. *J. Bact.* **41**: 301-303, 1941.

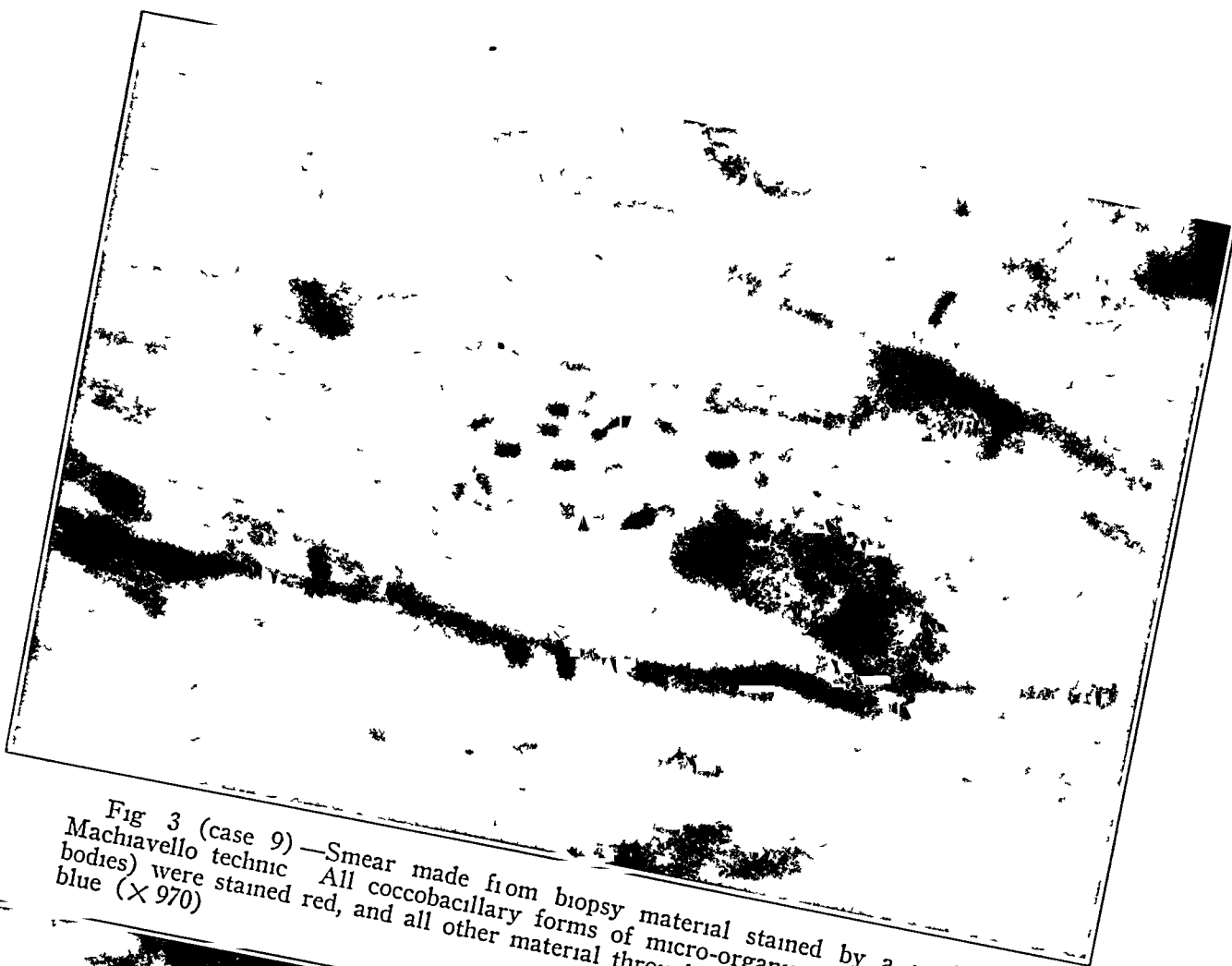


Fig 3 (case 9) — Smear made from biopsy material stained by a modified Machiavello technic. All coccobacillary forms of micro-organisms (deep-staining bodies) were stained red, and all other material throughout the smear was stained blue ( $\times 970$ )

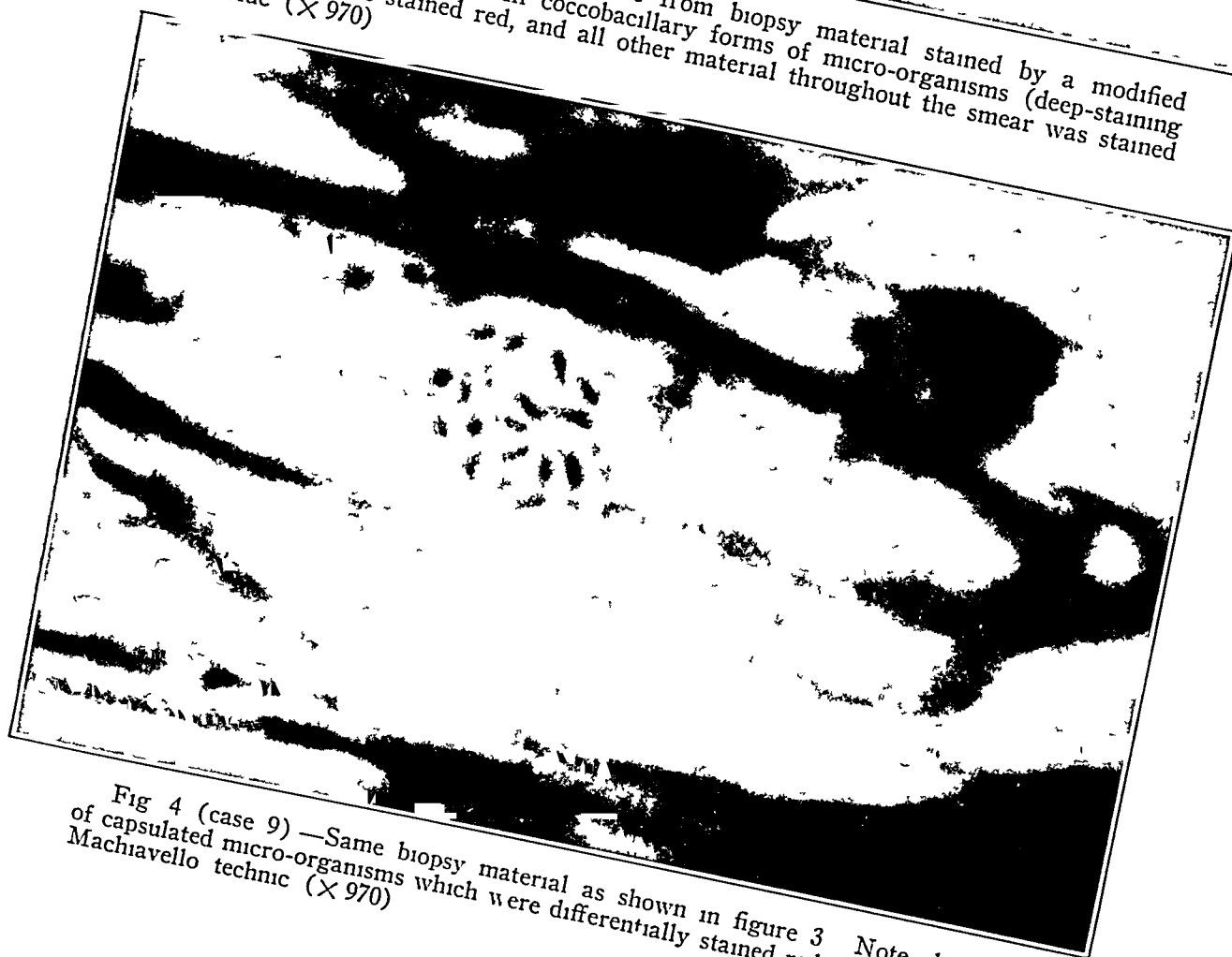


Fig 4 (case 9) — Same biopsy material as shown in figure 3. Note clusters of capsulated micro-organisms which were differentially stained red by the modified Machiavello technic ( $\times 970$ )

Smears made from these colonies and stained by the Gram method showed, in addition to staphylococci, rings and clusters of almost transparent bacillary forms of micro-organisms which, when examined under oblique illumination, appeared to be gram-negative, in striking contrast to the staphylococci (fig 2)

A subsequent biopsy was made in this case two months later, which afforded interesting data. Smears were made of the tissue and stained with Giemsa stain and also by a slightly modified Machiavello staining technic. The latter method showed small stout coccobacillary micro-organisms occurring singly or in small clusters which retained



Fig 5 (case 9)—Same biopsy material as shown in figures 3 and 4, showing a pathognomonic leishmania body stained by the modified Machiavello technic. The deep-staining forms were stained red, the paler forms and the cell nucleus were stained blue ( $\times 970$ )

the red color of the basic fuchsin. All other micro-organisms and organized structures observed were stained blue (fig 3). Occasionally some of these would appear as clusters of capsulated organisms of the same general size and shape and displaying the same staining characteristics (fig 4).

In other fields we observed such clusters of capsulated organisms which were apparently undergoing phagocytosis by large mononucleated cells (macrophages). Finally these red-staining capsulated micro-

organisms, intermingled with morphologically similar organisms which did not retain the basic fuchsin, could be seen within the cytoplasm of a mononuclear cell (stained blue) and gave the typical picture of a pathognomonic leishmania body (fig 5) The organisms not retaining the basic fuchsin stain may be nonviable forms

Similar microscopic observations were likewise obtained in cases 10 (fig 6) and 11

It seems possible that the capsulated forms represent the microorganisms covered with a layer of adsorbed serum, prior to phagocytosis



Fig 6 (case 10)—A 25 year old Negro man, married had had the disease for about six months Serologic tests for syphilis elicited negative reactions Frei and Ducrey tests elicited negative reactions Biopsy material removed from the penis when stained by the modified Machiavello technic showed conditions similar to those shown in figures 3, 4 and 5

In all cases in which there was failure to show any leishmania bodies there was also failure to show any rod forms which were morphologically similar or which retained the basic fuchsin stain when stained by the Machiavello method (cases 9, 10, 11, 14 and 15, table 1)

The modifications in the Machiavello method, as employed in the staining of rickettsias, were in time only The times used in our studies were as follows basic fuchsin, two and one-half minutes, citric acid five seconds and methylene blue one minute



## SUMMARY

Considerable evidence has been obtained which suggests that granuloma inguinale may be transmitted during coitus by means of infected pubic lice. It is not, however, suggested that this is the only means of transmission of the disease.

Our observations are in complete agreement with those of Anderson, DeMonbreun and Goodpasture that the etiologic agent of granuloma inguinale is a bacillus. We believe that the name *Donovania granulomatis*, as suggested by these investigators, would be a most appropriate one for this micro-organism.

Dr. Walter O. Teichmann, chief of the dermatologic clinic at Gallinger Municipal Hospital and associate professor of dermatology and syphilology at Georgetown University School of Medicine, referred several cases to us for study. Dr. Arnold H. Gould, fellow in dermatology and syphilology, Georgetown University School of Medicine and Hospital, referred case 9 to us. Major Charles R. Rein, chief of the division of serology of the Army Medical Center, made the serologic studies on several of these cases, the results of which studies appear in table. The personnel of the photographic laboratory of the Army and Navy Medical Centers contributed all photographic work appearing in this report.

## RHINOSCLEROMA

Observations Based on a Study of Two Hundred Cases

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**R**HINOSCLEROMA (scrofulous lupus of the nostrils, nasal scleroma) is a chronic disease of relatively benign evolution, whose contagiousness is doubtful, it is nonhereditary. Its anatomic characteristic is a tumor formation of varying volume, of waxy or reddish appearance and with a decided tendency to ulcerate and spread. It is invariably located in the rhinopharyngeal region.

### HISTORY

In the Museum of the History of Medicine, of Cracow, Poland,<sup>1</sup> there are wax models of this disease made in the year 1840, which were exhibited by Bierkowsky as cutaneous cancers. Hebra<sup>2</sup> (1870) was the first to make a clinical description of this curious disease, naming it rhinoscleroma (hard nose). At that time it was mistaken for syphilis and sarcoma. Geber<sup>3</sup> in 1872 and Mikulicz<sup>4</sup> in 1876 histologically demonstrated its sclerotic tissue. In 1882 Frisch<sup>5</sup> discovered an encapsulated bacillus which now bears his name and which he considered to be the main cause of the disease.

### INCIDENCE

Rhinoscleroma is widespread (more so than is generally supposed) in Europe, in Russia, Poland, Switzerland, Austria, Italy, Spain, Sweden and other countries. In North America there are a few cases to be found among immigrating races but rarely among natives. In South America, as well as in the West Indies, there have been several

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1 Watrin, J, in Darier and others. *Novelle pratique dermatologique*, Paris, Masson & Cie, 1936, vol 4

2 von Hebra, F. *Rhinosclerom*, Wien med Presse **11** 445, 1870

3 Geber, E. *Ueber das Wesen des Rhinosclerom, eine klinisch-histologische Studie*, Arch f Dermat u Syph **4** 491, 1872

4 Mikulicz, J. *Ueber das Rhinosclerom*, Arch f klin Chir **20** 485, 1876-1877

5 von Frisch, A. *Zur Aetologie des Rhinoskleroms*, Wien med Wchnschr. **32** 969, 1882

cases reported, however, it is in Central America (El Salvador and Guatemala) that cases of this disease are most frequently found

#### ETIOLOGY

Rhinoscleroma affects both sexes, but is predominant among women. In my experience with 200 patients, 120 were women. All of them were peasants, of poor hygienic habits, with the exception of 2 who proved to be city residents of doubtful hygienic habits.

The true agent causing this disease is not definitely known. It was attributed by Frisch to a bacillus of Friedlander type, which is to be found in regular quantities in some cases of rhinoscleroma. Notwithstanding, I have found this bacillus in patients attacked with rhinitis, without scleroma. It is probable that *Klebsiella ozaenae* and Friedlander's bacillus (*Klebsiella pneumoniae*) are present in large numbers in the pathologic conditions of these mucous membranes.

For many years I have tried to reproduce rhinoscleroma in laboratory animals, as well as in human beings, through inoculation and grafting, without success. Now my research work is focused on the theory that rhinoscleroma is caused by a filtrable virus.

The contagiousness of rhinoscleroma has been widely discussed, there are on record several cases which would appear to be a solution to the problem, such as those described by Lasagna, of 15 Italians who had rhinoscleroma (?), all of them members of the same family and dwelling in the same home. Among my cases, numbering 200, I have found only the case of 2 brothers who contracted rhinoscleroma, the one four months after the other.

#### BACTERIOLOGY

Frisch found in the nasal secretion from a person having rhinoscleroma an encapsulated diplobacillus, from 2 to 3 microns in length and from 0.5 to 1 micron in width, which when strained with Gram's stain appears light red and surrounded by a clear halo, the capsule. These characteristics do not belong exclusively to the Frisch bacillus (*Klebsiella rhinoscleromatis*) but belong to other encapsulated bacilli as well, such as the *K. ozaenae* and *K. pneumoniae*, which are found in the nostrils and which are responsible for adding to the confusion in establishing whether or not the Frisch bacillus is the real cause of this disease. Personally, I am of the opinion that the histologic and clinical observations are the only means of making the correct diagnosis of rhinoscleroma.

Cultures are made in gelose, and for this purpose an incision is made in one of the nodules and the blood flowing from the cut is used. The culture tube should be kept at a temperature of 37°. After twenty-four hours, small colonies begin to appear taking the shape of a button,

some are light yellow, and others are stearine white. Besides being made in gelose, cultures can be made in milk, on potato or in ordinary broth.

#### PATHOLOGY

The histopathologic structure of rhinoscleroma is characterized by three elements:

- 1 Plasmocytes infiltrate massively, occupying a large portion of the dermis and separating it from the epidermis by means of a thin zone of lymphatic cells.

- 2 Mikulicz cells, rounded elements, 50 microns in diameter, are found among the infiltrated plasmocytes. They appear pale, and almost transparent, with somewhat fading contours. In some of these cells the Frisch bacilli are to be found. In these cells is also noted a rounded curdling, which becomes intensely colored, is ordinarily located in the marginal zones and is classified as the nucleus. These cells are considered degenerated plasmocytes.

- 3 Strang elements, Russell bodies, also are found among the plasmocytic infiltration. They are from 20 to 40 microns in diameter and have been classified as degenerated hyaline bodies by Unna and Pellizari. These bodies are spherical and become intensely dark colored.

The histopathologic features of this disease vary in accordance with its different stages. Thus, for instance, in its secondary stage the presence of Russell bodies in regular quantities is also observed, in addition to the plasmocytic infiltration, while Mikulicz cells are very rare. The third stage is richer in details, at the beginning of this stage the Mikulicz cells start to be more abundant. The numerous dilated vessels are observed to have sclerosed walls, this sclerosis is sometimes so advanced that it completely obliterates the vessel. In more advanced cases of the third stage, a sclerotic tissue is noted as invading the entire field and segregating the plasmocytes in groups in which the Mikulicz cells are abundant, Russell bodies are rarely found here.

#### SYMPTOMATOLOGY

Rhinoscleroma is a chronic disease appearing in both sexes, predominantly among women. It makes its first appearance in persons between 20 and 40 years of age, being very rare among persons under 15 and over 50 years of age. The course of this disease, according to my statistical records, fluctuates between eight and twenty years.

The disease localizes itself in the rhinopharyngeal region, transforming the countenance of these patients to the extent of resembling a rhinoceros or a hippopotamus, it is never accompanied with fever. The patient's general condition is not affected, and the majority of persons

attacked are of the strong build type. It is hard to estimate accurately its period of incubation, and the development of its symptoms is gradual.

In view of the foregoing facts and for a better study of rhinoscleroma, I shall divide it into three stages.

*First Stage*—Rhinitis Period. In the majority of cases, the disease makes its appearance with all the symptoms of a coryza with fronto-ethmoidal cephalalgia, followed by rather difficult respiration, there is scant nasal secretion, more or less fetid. The patient complains of dryness of the throat. Rhinoscopic examination reveals a red mucous membrane already hypertrophic, that of the septum is particularly involved, as it is here that the infiltration first appears. While going through this period patients seldom call for medical advice and inexplicably will keep quiet about these troubles for months in succession. Most of the patients call on the physician for consultation only after the second period begins, that is, when mechanical phenomena appear (difficult respiration and others).

*Second Stage*—Infiltrating Period. The symptoms of coryza begin to disappear, leaving characteristic marks in those places where the infiltration localizes itself. In order of frequency these are nasal septum, lower part of the nostrils and larynx. The septum thickens to the extent of making respiration difficult, this obstruction being incomplete if it affects one side and total if it affects both sides. At the lower part of the nostrils there appear waxy or reddish infiltrations (fig *A*). Finally, laryngeal infiltration takes place, causing changes to occur in the modulations and intonations of the voice. In the majority of cases of the second period complete anesthesia of the soft palate is discovered, a sign that is diagnostic.

*Third Stage*—Nodular Period. This is the period of exaggerated or total spreading of the aforementioned second period. In this manner, then, rhinoscleroma localizes in the septum and progresses upward exaggerating the appearance of the nose and sometimes causing monstrous deformities, as shown in the figure (*B*). When the invasion progresses upward difficulty in respiration is not total, as the patient can inhale through the nose and the mouth. When the invasion progresses toward the bottom (floor) of the nostrils, it shows a decided trend to obstruct them completely, then the patient's voice takes on a deep twang, there are anosmia and epistaxis, the roof of the mouth becomes pale, and the palatal arch disappears, showing a tumor formation. The localization of the disease at the lower part of the nostrils shows a peculiar tendency to progress anteriorly, invading the lobe and wings of the nose, the upper lip and the alveolus. When the condition has reached this stage and the invasion is well advanced, the patient presents a repulsive appearance, as seen in the figures (*C* and *D*), resembling that of a hippopotamus. In such cases staphylococci

secondary infections are frequent, the lips become enlarged because of rhinoscleromatic infiltration, resembling the labia majora in cases of common elephantiasis due to venereal lymphopathies



Rhinoscleroma A, wavy nodules below nares B, advanced stage, showing rhinoceros-like projections C and D, advanced stages, showing hippopotamus-like projections

When laryngeal infiltration occurs, the patient's voice becomes bitonal, and as the infiltration progresses the voice disappears completely and respiration grows more painfully difficult to the extent of making

tracheotomy necessary. The process of scleromatous infiltration covers the larynx and pharynx, until some intercurrent disease causes death.

As stated before, these three periods take many years to reach full development. In some cases of localization in the nostrils, the growths ulcerate, yielding a yellow fetid secretion. When the disease is well advanced, these conditions are followed by destruction of bone which affects the septum and the superior and inferior conchas of the nose, as well as the maxillary and ethmoid sinuses.

In cases of rhinoscleroma, the hemogram presents no abnormalities.

There are cases on record, mainly those of the disease localized in the septum, in which there was a spontaneous regression, leaving behind an atrophy in the nose. I have observed such regression to occur, however, only during the first period of infiltration.

#### DIAGNOSIS

The diagnosis is based on the clinical appearance and on the histopathologic structure which are characteristics of this disease, thus differing from all other diseases of the skin (plasmocytic infiltration and Mikulicz cells). However, from the clinical standpoint, syphilis, ozena, sarcoma, mutilating rhinopharyngitis and snuffing goundou should be considered. In some cases, I have found false positive Wassermann reactions, there are also cases of combined syphilis and rhinoscleroma in which the preliminary treatment helps to establish the diagnosis. The differential diagnosis from sarcoma is made through coloration. The ligneous hardness, the painlessness, and slowness of evolution and the absence of ganglionic infarcts are diagnostic of rhinoscleroma. And, to complete the work, a complement fixation test may be resorted to, in view of the presence of Frisch's bacillus. The Forges-Elbert agglutination test as well as an intradermal test with toxin of Frisch's bacillus, may be tried.

#### PROGNOSIS

The disease is of long duration and curable, provided the patient calls on the physician at an early stage and provided the latter makes the diagnosis at the beginning of the period. Mortality varies in accordance with the localization and extension of the lesion. Thus, for instance, for patients with laryngeal localization with extension to the trachea asphyxia by obstruction is the constant threat and prompt intervention is required (tracheotomy) to save the patient's life. There may be recurrences, and when the disease is of long duration the patients may end with pulmonary tuberculosis, or the lesions may be transformed into malignant neoplasmas. In some cases, the lesions remain stationary, to become reactivated by some traumatism or infection.

## PROPHYLAXIS

Rhinoscleroma is a disease contracted through poor personal hygiene, it is never found among people of absolutely clean habits. Its contagiousness is doubtful. Among my cases and through my years of study of this disease, I have not yet encountered a single case that I could have unhesitatingly classified as contagious, I did, however, prove beyond any doubt that all my patients observed very poor hygiene both personal and in the home.

## TREATMENT

The monstrosity of this disease is responsible for innumerable treatments and procedures in the countries in which it is known to exist, it would take too long to enumerate them. All have no therapeutic value against this disease. Thus it happens that these patients have been treated with all sorts of mercurials, caustics (zinc chloride, lactic acid, pyrogallol, iodine, silver nitrate, salicylic acid), arsenicals, bismuth preparations, chaulmoogra oil, antimony and potassium tartrate, vaccines (autovaccines), autohemotherapy, proteinothérapie, interstitial injections of iodine, methylthionine chloride, electrocoagulation, cautery, surgical extirpation, curettage or the so-called pruning system. After the last system has been applied, the infection progresses with greater aggressiveness.

Among my cases, the only treatment giving excellent results, to the extent of permitting this disease to be considered curable, is roentgen irradiation, given in sessions of seven applications with the following technical factors: 200 kilovolts, filtered through 0.5 mm of copper and 1 mm of aluminum, focal skin distance, 50 cm, dose, 200 r per day, during seven consecutive days, total dose, 1,400 r and fields, one antero-posterior over the nose. The reaction is light erythema, followed by hyperpigmentation which disappears after three months.

Five applications should be given per year during the first and second stages, for two years. In the third stage, the prognosis for complete healing is reserved, but I have succeeded in keeping my patients in good condition, so that they could work and keep on living their routine, normal lives.

Surprising results have also been obtained through intramuscular injections of azosulfamide (disodium 4-sulfamidophenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene 3', 6'-disulfonate).

In conclusion, at the present time the only effective therapeutic agents to combat rhinoscleroma are roentgen rays and azosulfamide.



## MAMMALIAN PIGMENTATION

The Problem of the Pigmentary Mechanism Studied by Means of the  
Respiration of Tissues

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AND

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**T**HE MECHANISM of pigmentation in the lower animals has been fairly well established. Some of the precursors of the melanin compounds have been isolated, and the enzyme tyrosinase has frequently been identified in extracts from tissues of these lower animals. In them, it is thought that the formation of melanin proceeds from the naturally occurring amino acid tyrosine and involves enzymatic catalysis, with tyrosinase as the active enzyme. Raper and Evans<sup>1</sup> gave a logical series of enzymatic and chemical reactions for the pigmentation mechanism.

However, tyrosinase has rarely been isolated from pigmented tissues of mammals, with the result that considerable confusion exists concerning the enzyme active in mammalian pigmentation. Bloch's<sup>2</sup> extensive work on the pigmentary mechanism in the human being led many to favor his theory of the existence of a special oxidase (dopase)-producing melanin in human beings by action on a prepigment *l*-3, 4-dihydroxyphenylalanine (dopa). On the other hand, Meirrowsky<sup>3</sup> came to the conclusion that no dopa oxidase exists, preferring to accept an unspecific polyphenoloxidase or a chemically characterized catalyst as a more likely actor in the production of melanin. Schaaf,<sup>4</sup> too, suggested a similar

This research was made possible partly through a grant from The Doctor Simon Baruch Fund.

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University, and the Institutum Divi Thomae, Cincinnati.

1 Raper, H. S. Some Problems on Tyrosine Metabolism, *J. Chem. Soc.*, 1938, pp. 125-130. Raper, H. S., and Evans, W. C. A Comparative Study of the Production of *l*-3, 4-Dihydroxyphenylalanine from Tyrosine by Tyrosinase from Various Sources, *Biochem. J.* **31**, 2155-2170, 1937. Evans, W. C., and Raper, H. S. The Accumulation of *l*-3, 4-Dihydroxyphenylalanine in the Tyrosinase-Tyrosine Reaction, *ibid.* **31**, 2162, 1937.

2 Bloch, B. The Problem of Pigment Formation, *Am. J. M. Sc.* **177**, 609-618, 1929.

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mechanism, for he found that extracts of skin oxidize not only dopa but also catechol, hydroquinone, *d*-3,4-dihydroxyphenylalanine and at times even *p*-cresol

Recently, Hogeboom and Adams,<sup>5</sup> using extracts from the Harding-Passey mouse melanoma, a tumor composed of melanin-producing cells, showed that enzymes were present which oxidized dopa and *l*-tyrosine. They obtained two fractions, one of which was active in oxidizing dopa but was unable to oxidize tyrosine, hydroquinone and *p*-cresol, and the other an insoluble fraction which oxidized tyrosine but failed to oxidize phenol, hydroquinone and *p*-cresol.

The present studies include use of the Harding-Passey mouse melanoma. We worked with the tissue itself rather than with extracts. It is hoped that thereby the *in vivo* essentials of the enzymes or catalysts present in the tissue are preserved. In order to control the interpretation of the results, identical studies with nonpigmented tumors were also made.

#### PROCEDURE

Tissue slices of the Harding-Passey mouse melanoma were used in the studies of the pigmentary process, comparable studies were made with tissue slices of mouse sarcoma 180 of albino mice, the Bar Harbor adenocarcinoma of dba mice and the ears of guinea pigs. All the animals were killed by a sharp blow over the base of the skull. The tissues were removed immediately and placed in Ringer's solution (0.2 per cent dextrose). The solution was buffered to *p*<sub>H</sub> 6.5, instead of the usual 7.3, in order to prevent auto-oxidation of the dopa solutions used in some of the experiments.

The tissues were carefully freed of all connective tissue and cut into sections approximately 1 cc. in volume, and the sections were placed in the manometer flasks. The respiration was measured at 37.5 C. in air, by the direct method,<sup>6</sup> the constant volume type of Warburg manometer being used. Seven manometers were used in the experimental runs, one for the thermobarometric control and the remaining six for tissue controls and for testing the effects of added solutions.

The solutions to be tested were placed in the side arms of the manometer flasks. After an equilibrium period of fifteen minutes, the oxygen consumption of the tissue was measured during a control period of forty-five to sixty minutes, readings being taken every fifteen to thirty minutes. Then the test solutions were tipped into the flasks from the side arms, and the oxygen consumption was measured for one and a half hours, readings again being taken every fifteen to thirty minutes. The tissues were then carefully removed from the flasks, washed in distilled water and dried to a constant weight at 100 C. From 25 to 35 mg. (dry weight) of tissue was used in each flask. The carbon dioxide produced by the tissues was measured "by rates,"<sup>7</sup> the direct method again being used. The solutions tested were (1) dopa, 0.05 and 0.1 per cent, (2) potassium cyanide

<sup>5</sup> Hogeboom, G. H., and Adams, M. H. Mammalian Tyrosinase and Dopa Oxidase, *J. Biol. Chem.* **145** 273-279, 1942.

<sup>6</sup> Dixon, M. Manometric Methods, ed. 2, New York, The Macmillan Co., 1943.

<sup>7</sup> "By rates" refers to the manner of recording the amounts of carbon dioxide liberated in a series of successive fifteen minute intervals of time.

and (3) sodium fluoride, each 0.001-molar and 0.01-molar, (4) *p*-cresol, 3 mg and 5 mg. The values given for these substances refer to the concentrations or the quantities present in the manometer flasks after these solutions were tipped from the side arm.

## RESULTS

The results given in table 1 show that with the mouse melanoma dopa invariably stimulates the uptake of oxygen and the liberation of carbon dioxide. This points to an enzymatic rather than to a simple chemical catalytic operation in the oxidation of dopa. The increased production of carbon dioxide suggests further that there is in the tissue

TABLE 1—*Influence of Dopa on the Respiration of Melanoma Tissue (Harding-Passey Mouse Melanoma)*

Period *	Melanoma, Cu Mm per Mg per Hr		Melanoma + Dopa 0.1% Cu Mm per Mg per Hr	
	Q O <sub>2</sub>	Q CO <sub>2</sub>	Q O <sub>2</sub>	Q CO <sub>2</sub>
Control	0.545	0.263	0.468	0.366
Experimental	0.426	0.217	0.953	0.503
Per cent change—experimental over control	—22	—17	+104	+42

\* The words "control" and "experimental" as referable to the periods of respiration refer to the first and the second halves of the respiration run, during the latter of which dopa was added to some of the melanoma tissue.

TABLE 2—*Influence on the Uptake of Oxygen of Tissue on Addition of Dopa, Potassium Cyanide (KCN) and Sodium Fluoride (NaF)\**

Tissue	Dopa 0.05% Con- centration	KCN 0.01 M Con- centration	KCN + Dopa 0.01 M + 0.05% Concentration	NaF 0.01 M Con- centration	NaF + Dopa 0.01 M + 0.05% Concentration
Mouse melanoma	+63%	—56%	—61%	—51%	+21%
Mouse adenoma	—17%	—28%	—40%	—76%	—81%
Mouse sarcoma 180	—33%	—53%	—44%	—69%	—76%
	(a) 0.05% Conc (b) 0.1% Conc	0.001 M Conc		0.001 M Conc	
Guinea pig skin (ear)	(a) —15% (b) +11% within experi- mental error	—54%	—56%	—19%	—26%

\* Expressed as percentile stimulation (+) or inhibition (—) of the control tissue respiration.

a substrate akin to dopa and/or that a redox system operates within the mechanism of pigment formation.

As revealed by table 2, dopa causes an inhibition of the oxygen uptake of the nonpigmented tumors, both sarcoma 180 and the adenoma. This strongly suggests that dopa's stimulation of the respiration of the melanoma is connected with the pigmentary process. The addition of potassium cyanide and sodium fluoride causes an inhibition of the uptake of oxygen in all tissues. The same depression tends to prevail after dopa is added to the mixtures containing potassium cyanide and sodium fluoride. However, note should be taken of the fact that when

dopa was added to the mixture containing sodium fluoride the latter failed to suppress completely the stimulation expected from dopa. These observations are further indications of an enzymatic process.



Photomicrograph showing the Harding-Passey mouse melanoma. The melanotic growth is so infiltrated by melanin particles as to mask completely in places the cells that produce these particles.

underlying the oxidation of dopa and, under the conditions of the experiments, of the sensitivity of the enzyme to cyanide and fluoride poisoning.

Attention is called to the feeble response of the skin (the ear of a guinea pig) following exposure to dopa. Efforts to study the pigmentary process in healthy skin by the monometric procedure have repeatedly given measurements within the limits of experimental error, and this fact directly accounts for the necessity of resorting for study to the type of tissue (melanoma) reported on in this paper. Normal skin obviously contains too little of the pigmentary materials to reveal meaningful data by procedures now available.

Mouse melanoma *B16* (pulp) disclosed an almost complete loss of capacity to take up oxygen, but addition of dopa caused a considerable increase in the uptake of oxygen. The further addition of potassium cyanide caused complete inhibition of this stimulation. Here, too, is supportive evidence of an enzymatic process in the oxidation of dopa.

Several experiments with mouse melanoma and added *p*-cresol gave equivocal results, at times a stimulation of respiration and at others a depression. The production of carbon dioxide was regularly depressed. This experiment sought to discover evidence in behalf of tyrosinase as the enzyme concerned in these reactions. It may well be that significant variations in the concentrations of the enzymes in the several melanoma tissues used accounted for the contradictory findings.

#### SUMMARY

The data presented lead to the following conclusions in respect to the pigmentary process in mammals:

- 1 The process requires an enzymatic step
- 2 Dopa may be the actual prepigment involved
- 3 No definite conclusions can be drawn as to the specific character of the enzyme in operation, although the evidence suggests the presence of tyrosinase

As referable to the character of the enzyme, attention is directed to the fact that these studies were carried out with the solution containing the tissues at a  $p_H$  of 6.5, probably nonoptimal for the process under investigation. While this degree of acidity was used to prevent auto-oxidation of dopa, it may have interfered with attempts to elicit distinguishing characteristics of the enzyme.

# DIAGNOSTIC SIGNIFICANCE OF THE CULTURE METHOD IN CUTANEOUS LEISHMANIASIS (ORIENTAL SORE)

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JERUSALEM, PALESTINE

CULTURES of the leishmania parasite were first made by Nicolle,<sup>1</sup> and the customary method is to use on the N N N (Nicolle Novy-McNeal) medium. Culture is, however, as a rule, used for laboratory transmission and therapeutic experiments while only rarely has it been employed as an aid in clinical diagnosis.

In countries where the disease occurs endemically there are always numerous cases which, although clinically they may arouse the suspicion of leishmaniasis, require confirmation by objective methods by which the parasite can be demonstrated. This applies particularly to the ulcerative lesions of long standing and to relapsing leishmaniasis, in which it is generally impossible to demonstrate the parasites in smear preparations. In these recurrences which clinically show a striking resemblance to lupus and to tertiary syphilis and in which it is equally difficult to discover the parasites, it is of greatest importance to be in possession of a method by which it is possible to establish an objective diagnosis. Neither can the histologic picture, which in these types often has a tuberculoid structure, be used to decide the differential diagnosis.

We have, therefore, in a number of cases studied the diagnostic significance of the culture method and are, in the following presentation, giving the results of these studies.

## EXPERIMENTAL SETUP

We used Adler's modification of Noguchi's medium<sup>2</sup> consisting of

	Parts
Agar (2.5 per cent)	1
Locke's solution containing 0.1 per cent of dextrose	8
Fresh rabbit blood	1

From the Dermatological Department of the Hadassah-Rothschild University Hospital, Jerusalem, Palestine, Dr. A. Dostrovsky, Director

1 Nicolle, C. Culture du parasite du bouton d'Orient, *Compt rend Acad d sc* **146** 842, 1908

2 Adler, S., and Theodor, O. The Identity of *Leishmania Tropica* Wright, 1903, and *Hepetomonas Papatasi* Adler, 1925, *Ann Trop Med* **20** 355-364 (Dec 17) 1926

(In some cases the specimens were taken, and cultures set up in the hospital, the cultures, however, were transferred for further bacteriologic study to the Bacteriologic Institute [Director Dr Gurevitch] while in others the patients were sent to the Parasitologic Institute [Director Professor Adler] and the whole process of culturing carried out there.) Specimens were taken by making small cuts into the lesion, usually at the edge in no case in the suppurating or ulcerating center. A small glass capillary tube to which a rubber ball was attached was then placed into one of these cuts. Since the prospects of obtaining positive cultures from blood alone are negligible, it was tried, by slight to-and-fro motion with simultaneous aspiration, to detach minute shreds of tissue. The material thus obtained was then transferred to the culture medium and kept at a temperature of 22 C. Complete sterility is important, since the culture medium is susceptible to contamination. Several tubes should be inoculated at the same time. If the parasites are numerous, they grow on the cultures within the course of a week. In the cases referred to, in which the smears contained no or only isolated parasites, so that their identification was impossible, a definitely positive culture occasionally required as long as three weeks.

*Subjects*—The total number of cases in which cultures were made was 61, in several of which the procedure had to be repeated after a negative result had been obtained on the first occasion.

The first group, comprising 26 cases, was of the early stage of leishmaniasis, while a further 30 were of recurrent leishmaniasis, and in 5 the material was obtained from scars after healing had already taken place.

#### RESULTS

In 10 cases in which smears yielded positive results, cultures were also invariably positive. In two of the positive smears, the cultures showed secondary infection, hence the results were negative. In 8 cases which were in the last few months before spontaneous healing could be expected to take place and in which microscopically no parasites

TABLE 1—*Comparison of Results in Smear Preparations and in Cultures in 26 Cases of the Early Stage of Cutaneous Leishmaniasis*

	Number of Cases
Positive in smears and cultures	10
Positive in smears negative in cultures	2
Negative in smears, positive in cultures	8
Negative in smears negative in cultures	6
Total	26

were found, cultures were still positive. In the remaining 6 cases in which cultures as well as smears were negative three cultures showed repeated contamination, one was of the annular type of leishmaniasis with only a positive cutaneous reaction and two remained negative although there was no contamination. Contamination usually occurred in material taken from suppurating boils, so that clean material could not be obtained even from the edge of the lesion. These early types with

their frequent secondary infection offer much technical difficulty, while, on the other hand, this is of no consequence, since in such cases the differential diagnosis is more rarely fraught with difficulty

Conditions are different in cases in which long-standing lesions or recurrences in long-standing scars are concerned

In connection with the question of recurrence *in loco*, we studied 5 cases of cutaneous leishmaniasis which, from a clinical viewpoint, could be declared as cured. Cultures as well as smears were negative

TABLE 2—Comparison of Results in Smears and Cultures in Thirty Cases of the Late Stage of Cutaneous Leishmaniasis (*Leishmaniasis Recidiva*)

	Number of Cases
Positive in smears, positive in cultures	2
Positive in smears, negative in cultures	0
Negative in smears, positive in cultures	18
Negative in smears, negative in cultures	10
Total	30

in all of them, while the intracutaneous leishmania vaccine elicited a positive reaction

In 1 of the cases cultures were exclusively set up for the purpose of demonstrating that healing had actually taken place, so that there remained 29 cases with an active process. Cultures were positive in 20 of them and negative in 9. In the smears, parasites were found in 2 instances only, and it must be pointed out that no more than one or two parasites could be detected and this only after a search of several hours. Only an experienced examiner was able to identify them as leishmania parasites at all.

In 60 per cent of this group, therefore, definite evidence of the leishmania nature of the lesion was supplied by the culture method alone.

This is illustrated by the following cases

#### REPORT OF CASES

CASE 1—The patient was a boy of 11 years. He was born in Baghdad. When he was 2 years old, he had had two lesions on the right forearm, now marked by two scars. We were probably dealing with healed lesions of leishmaniasis. Since his seventh year, he had had a lesion on his nose (fig. 1).

*Examination*—There was a lesion occupying the entire distal portion of the right half of the nose, here and there spreading to the left side consisting of flat infiltrations dissolving at the outer border into isolated small papules. To the right of the tip of the nose there was a slightly elevated area of granulation. The infiltrations had a reddish brown tinge. In one place scar tissue was noted. Pressure by a glass spatula revealed a multitude of tiny papules of a yellowish tinge in the depth.

A Mantoux test (old tuberculin in a dilution of 1:50,000) elicited a positive reaction. A test with *Leishmania* vaccine elicited a positive reaction. Microscopic



examination revealed no bacteria. Growth of *Leishmania* parasites appeared on cultures after three weeks.

*Comment*—The localization and the aspect of the lesion confronted us with a differential diagnosis between cutaneous leishmaniasis and lupus vulgaris. No parasites could be demonstrated, but the intracutaneous test for leishmaniasis



Fig 1—Lupus-like leishmaniasis. Culture was positive for *Leishmania* parasites.



Fig 2—Serpiginous recurrent leishmaniasis. Microscope revealed no parasites but culture was positive.

elicited a positive reaction. Since, however, the patient had already had a leishmania lesion on his forearm when he was 2 years old, the result of the test was not decisive. The tuberculin test elicited an equally positive reaction. Thus only the identification of the parasites in the cultures provided the decisive evidence.

**CASE 2**—The patient was a 12 year old girl who was born in Baghdad and had been in Palestine for seven years. She presented lesions on both cheeks, which had been present since the age of 1 year.

*Examination*—The patient (fig 2) presented on the anterior portion of the right cheeks two coalescing lesions consisting of a reddish brown infiltration with serpiginous spread to the periphery, while in the center spontaneous healing had already set in. Below this lesion there was an oval, sharply outlined scar with a small infiltration at one point of the edge, and above there was a second, smaller, scar with beginning infiltration. To the right of the mouth, there was a small punched scar. The left cheek offered essentially the same aspect, though of lesser intensity.

A Mantoux test (old tuberculin in a dilution of 1:50,000) elicited a negative reaction. An intracutaneous test with a leishmania vaccine elicited a positive



Fig 3—Recurrent leishmaniasis with no parasites and rare localization on the lips. Cultures were positive for the parasites.

reaction. There were no leishmania parasites in smears (three examinations). *Leishmania bacteria* grew on culture.

*Histologic Examination* (Pathological Institute, Director Professor Franco) — Granulation tissue of a tuberculoid type was found with typically tuberculous structure without caseation. Examination revealed no *Mycobacterium tuberculosis* and leishmania parasites.

*Comment*—The patient presented lesions which, clinically, bore much resemblance to the serpiginous type of lupus. The scars which were sharply punched with their recurrent papules were, here in this country, suggestive of cutaneous leishmaniasis. The objective evidence was supplied only by the cultures, since no parasites could be demonstrated either in smears or by histologic examination.

**CASE 3**—The patient was a girl of 15, born in Baghdad. For seven years she had had lesions which grew slowly. She had received injections (antimony?) and roentgen ray therapy but without effect.

*Examination*—There were seven lesions on the face (fig 3) on the forehead, the nose, the upper and lower lips and the outer angle of the right eye as well as two on the left cheek. All the lesions showed distinct reddish brown infiltrations which, on the nose, showed a tendency to ulceration with serpiginous spread on the cheek. There were two similar lesions on the arm and two on the leg.

A Mantoux test (old tuberculin in a dilution of 1:50,000) elicited a positive reaction. An intracutaneous test with leishmania vaccine elicited a positive reaction. Several examinations revealed no parasites. Culture was positive for *Leishmania* after three weeks.



Fig 4—Recurrent leishmaniasis appearing in gumma fashion, with parasites present on culture.

*Histologic Examination* (Professor Franco)—“The epidermis of the lesion on the arm is hypertrophied. The cutis contains several circular lesions, lying very close together and showing a granulomatous structure similar to that of chronic tuberculosis without caseation. Langhans' giant cells are present in abundance. No *Leishmania* parasites can be demonstrated.”

*Comment*—The patient presented a total of eleven lesions on various parts of her body. Although the clinical aspect was typical of recurrent leishmaniasis, the histologic picture and the reaction to the tuberculin test were in an equal measure suggestive of tuberculosis, and it was only by the positive results of cultures that the bacteriologic evidence could be provided.

**CASE 4**—The patient was an Arabian boy, aged 17, from Ramallah, a small town in the neighborhood of Jerusalem. Three years earlier a small papule had developed on his right cheek, which grew and ulcerated rapidly. In the course of one year, however, healing was complete. A short time later new lesions appeared on the right as well as on the left cheek, which spread systematically,

leaving pigmented scarring. When we saw the patient, both cheeks, particularly the left, were involved (fig 4). There was active infiltration of the edges in the neighborhood of the eyes and nose, while on the opposite side, toward the mandible, the lesions had already disappeared leaving scars. The spread was similar to that of tertiary syphilis. The entire upper lip was swollen to twice its original size and occupied by a deep infiltration, here and there spreading to the red portion. A similar lesion existed on the left auricle.

An intracutaneous test with *Leishmania* vaccine elicited a positive reaction. There were no *Leishmania* parasites in smears. Cultures were positive for *Leishmania* parasites. Wassermann and Kahn reactions were negative.

Histologic examination of specimens from the right cheek and ear revealed tuberculoid granulation tissue.

*Comment*—The patient presented lesions on the cheek and on one ear, spreading in a typical serpiginous way and forming reddish brown infiltrations in gumma fashion. No parasites could be demonstrated in the smears, and in the histologic examination no distinction from tuberculosis or gumma was possible. The reaction of the intracutaneous test as well as the cultures were positive for leishmaniasis.

#### COMMENT

In 61 cases of cutaneous leishmaniasis (Oriental sore) cultures for diagnostic purposes were set up. Although in the majority of the cases it could be assumed, in view of the clinical aspect and the results of diagnostic methods (histology, reaction to *Leishmania* vaccine, history, etc.) especially here in this country that we were dealing with cutaneous leishmaniasis, the final evidence was still lacking. Among 26 cases of early disease the parasites could be demonstrated exclusively by culturing in 8 instances, and the same was true in 18 out of 30 cases of recurrent leishmaniasis. Five of the patients presented scars after healing had already taken place.

Although the data are not numerous, they clearly underline the diagnostic significance of the culture method.

The difficulty of demonstrating the parasites in smears in the clinically deviating types of cutaneous leishmaniasis has repeatedly been stressed. Dostrovsky<sup>3</sup> reported positive evidence of parasites in only 1 out of a group of 6 cases of recurrent leishmaniasis. Maschkileisson, Neradov and Rapoport<sup>4</sup> were unable to detect parasites in any of their 9 cases of lupoid leishmaniasis. Berlin<sup>5</sup> reported positive findings in 3 among 13 cases. Smith<sup>6</sup> pointed out that in late recurrences

3 Dostrovsky, A. Relapses in Cutaneous Leishmaniasis, *Ann Trop Med* 30 267-274 (Oct 21) 1936.

4 Maschkileisson, I., Neradov, L., and Rapoport. Étude clinique et histologique de la leishmaniose cutanée boutonneuse (leishmaniose lupoides), *Ann de dermat et syph* 6 229-241 (March) 1935.

5 Berlin, C. Leishmaniasis Recidiva Cutis, *Leishmanid*, *Arch Dermat & Syph* 41 874-886 (May) 1940.

6 Smith, J. F. Late Cutaneous Recurrence of South American Leishmaniasis After Treatment with Antimony. *Brit J Dermat* 54 231-234 (Aug-Sept) 1942.

of American leishmaniasis parasites are scarce or altogether undetectable. The same difficulty was encountered by Marchionni<sup>7</sup> in the atypical manifestations in cases of long standing. As a general rule, the demonstration of parasites seems to be particularly difficult in South American leishmaniasis. Garzon and Molina,<sup>8</sup> therefore, based their diagnoses on the clinical aspect, the differential diagnostic distinction from other lesions and the success of treatment with antimony and potassium tartrate, and it should be assumed that in these types the culture method would be of particular diagnostic significance.

Gitelzon<sup>9</sup> found among 3,197 cases 89 of "meta-leishmaniasis." Among our 600 cases of leishmaniasis, 62 were cases of recurrence, in which as a general rule smears contain no parasites, and to this number at least 10 per cent of the nodular and especially of the ulcerative early types should be added, in which it is impossible to detect the parasites even by repeatedly preparing smears. Behdjiet<sup>10</sup> pointed out that in 4 per cent of his cases after healing had taken place tuberculous lesions appeared at the original site of the lesion. Probably he was dealing with recurrent leishmaniasis in which no parasites could be demonstrated, and the same applies to Sinderson<sup>11</sup>. The so-called lupus developing in leishmaniasis scars, according to these authors, probably would have been identified as a late leishmaniasis lesion if the appropriate culture method had been applied.

In view of the foregoing statements, it is all the more significant that in a number of dermatologic textbooks no mention is made of the culture method for diagnostic purposes (Sutton and Sutton,<sup>12</sup> Ormsby and Montgomery,<sup>13</sup> "Nouvelle pratique dermatologique,"<sup>14</sup>

7 Marchionni, A. Die Behandlung der Orientbeule (Hautleishmaniose), *Schweiz med Wchnschr* **71** 1220-1223 (Oct 18) 1941.

8 Garzon, R., and Molina, R. J. A proposito de un caso de Leishmaniosis tegumentaria americana, consideraciones clinicas diagnosticas y terapeuticas, *Rev argent dermatosis* **26** 225-247, 1942, cited by Wise, F., and Sulzberger, M. B. 1942 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1942, p. 142.

9 Gitelzon, I. I. (a) Atypical Forms of Cutaneous Leishmaniasis, *Sovet vestnik venerol i dermat* **1** 34-36, 1932, (b) Skin Leishmaniasis, Ashkhabad, Turkmenistan Government, 1933, cited by Berlin.<sup>5</sup>

10 Behdjiet, H. A propos des boutons de Wright, in *Deliberationes congressus dermatologorum internationale IX-1*, Leipzig, Johann Ambrosius Barth, 1936, vol. 2, p. 598-605.

11 Sinderson, H. C. Lupus Vulgaris and Oriental Sore, *Tr Roy Soc Trop Med & Hyg* **25** 75-76 (June) 1931.

12 Sutton, R. L., and Sutton, R. L., Jr. Diseases of the Skin, St. Louis, C. V. Mosby Company, 1943.

13 Ormsby, O. S. and Montgomery, H. Diseases of the Skin, Philadelphia, Lea & Febiger, 1943.

14 Vigne, P. Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 3.

etc.) Mayer and Nauck<sup>15</sup> wrote, in Jadassohn's Handbook, schematically that a diagnosis through culturing is only rarely deemed necessary, without entering on further details regarding that point.

In a few monographs only, dealing with tropical diseases, culturing is mentioned as a diagnostic method (Rogers,<sup>16</sup> Reed,<sup>17</sup> Manson-Bahr<sup>18</sup>). But even these authors failed to supply detailed information as to the significance of the method in the various types of the disease. The question seems to have gained great importance in this war, since the disease has spread considerably as a result of troop contingents passing through the Near East, and it is probable that atypical cases may turn up in nonendemic countries too, even after years. Recently Goldman,<sup>19</sup> in a review dealing with the preparation of the material for diagnostic purposes in various tropical dermatoses, described the technic of obtaining the material and emphasized the importance of the culture method for the diagnosis of leishmaniasis.

The few experiments outlined in the foregoing paragraphs seem to us to indicate that greater importance should be attached to the culture method for the diagnosis of leishmaniasis of endemic as well as of nonendemic spread than has so far been the case.

#### SUMMARY

The varied clinical picture of cutaneous leishmaniasis makes an objective diagnostic method a matter of greatest importance. Especially in the atypical and particularly in the late types of this disease, the microscopic demonstration of parasites often fails.

The results in 31 cases of leishmaniasis nodosa and leishmaniasis ulceroosa and in 30 cases of leishmaniasis recidiva have been used in evidence of the possibility that parasites can be demonstrated in cultures. In 26 cases the cultures were the only means of establishing the presence of parasites. Insufficient attention is being attached to this laboratory method as a diagnostic means in the textbooks on dermatology and, to some extent, in those dealing with tropical diseases.

Professor Adler and his assistant, Mr. Bar, of the Parasitological Institute of the Hebrew University, Jerusalem, Palestine, and Dr. Gurevitch, Head of the Bacteriological Institute of the Hadassah-Rothschild University Hospital, Jerusalem, Palestine, assisted with this paper.

15 Mayer, M. and Nauck, E. G. Leishmaniosen der Haut und Schleimhaute, in Jadassohn, J. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 12, pt. 1.

16 Rogers, L., and Megaw, J. W. D. Tropical Medicine, London, J. & A. Churchill, Ltd. 1930.

17 Reed, A. C. Tropical Medicine in the United States, Philadelphia, J. B. Lippincott Company, 1930.

18 Manson-Bahr, P. H. Manson's Tropical Diseases, London, Cassel & Co., Ltd., 1942.

19 Goldman, L. Preparation of Material for Laboratory Diagnosis of Some Tropical Diseases of the Skin. Arch. Dermat. & Syph. 50: 264-266 (Oct.) 1944.

## ASPERGILLUS INFECTION OF THE NAILS

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ASPERGILLI when found in mycologic cultures of the skin and of the nails have long been considered incidental clinic or laboratory contaminants and of no pathogenic significance. However, increasing evidence over the past twenty-five years has led to the realization that species of this genus of the fungi might actually be primary or secondary invaders of the human nail.<sup>1</sup> In 1941 one of us (E S B) had the opportunity to investigate a case of primary invasion of the human nail by a species of *Aspergillus*. In this case each time nail scrapings were cultured they yielded large numbers of colonies of *Aspergillus flavus*, but no other species of fungus was recovered. It was observed in this case that the infected nail plate had a dull green discoloration in addition to the usual characteristics of onychomycosis, such as thickening, brittleness, vertical striations and crumbling of the distal portions. The organism on culture had a yellowish green color. It was therefore believed that the discoloration of the nail was caused by the abundant growth of the fungus in the heavily infected portions of the nail plate. A direct examination of the nail plate in a

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1 (a) Émile-Weil, P, and Gaudin, L. Contribution a l'étude des onychomycoses. Onychomycoses a *Penicillium*, a *Scopulariopsis*, a *Sterigmatocystis*, a *Spicaria*, Arch de med exper et d'anat path **28** 452, 1919 (b) Sartory, A. Sur un champignon nouveau du genre *Aspergillus* isolé dans un cas d'onychomycose, Compt rend Acad d sc **170** 523, 1920 (c) Ota, M. Sur une nouvelle espèce d'*Aspergillus* pathogène. *Aspergillus jeanselmei* n sp, Ann de parasitol **1** 137, 1923 (d) Sartory, A, Sartory, R, Hufschmitt, G, and Meyer, J. Un cas d'onychomycose provoquée par un *Lurotium* nouveau. *Eurotium diplo-* cyste n sp, Compt rend Soc de biol **104** 881, 1930 (e) Smith, L M. *Aspergillus* Infection of the Nails, Urol & Cutan Rev **38** 783, 1934 (f) Bereston, E S, and Keil, H. Onychomycosis Due to *Aspergillus Flavus*, Arch Dermat & Syph **44** 420 (Sept.) 1941 (g) Rockwood, E M. A Study of Fungus-Infected Nails, ibid **22** 395 (Sept.) 1930 (h) Bereston, E S, and Waring, W S. Onychomycosis and Dermatomycosis caused by *Trichophyton Rubrum* and *Aspergillus Nidulans*, Arch Dermat & Syph **52** 162, 1945

10 per cent solution of potassium hydroxide revealed considerable hyphae and spores characteristic of *Aspergillus*. The organism obtained on cultures was identified by Dr Charles Thom, leading authority on the *Aspergilli*, as *A. flavus*. Cultures of the organism were obtained repeatedly from many specimens of the infected toe nail. A photomicrograph of the strain *A. flavus* isolated in this case is shown in fig 1

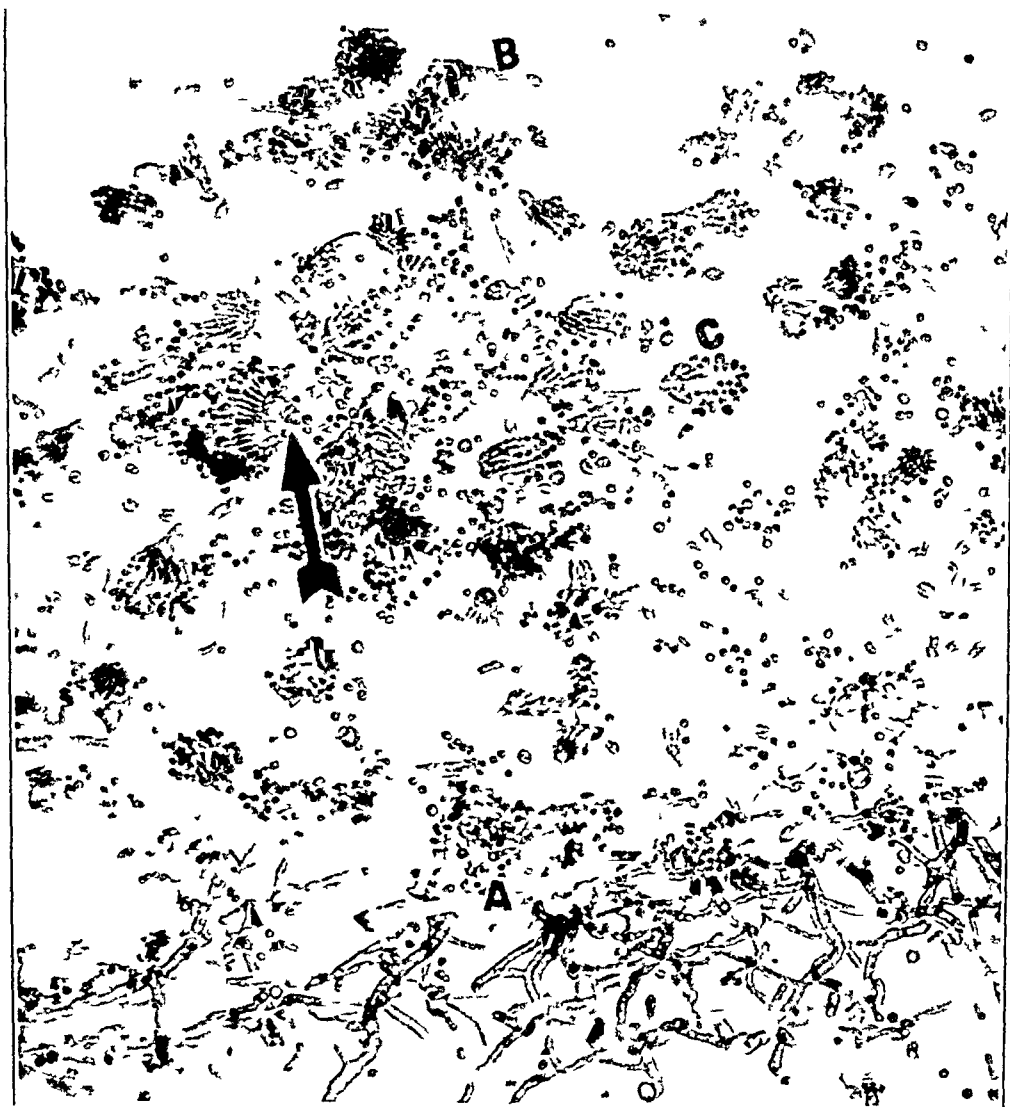


Fig 1—Microscopic cultural appearance of *Aspergillus flavus*. A indicates the level of the surface. Just below the surface the hyphae are seen in abundance. B shows a conidiophore ending in a balloon-like vesicle, seen best at the point of the arrow. The circumference of the vesicle shows a single file of sterigmata, from which straight lines of spores or conidia issue (C).

Recently we reported a case of multiple infection of the finger nails and toe nails with *Trichophyton rubrum* and *Aspergillus nidulans*.<sup>11</sup> In this case a number of specimens from the infected nails were obtained on seven different occasions during a period of two months. Culture of



these specimens produced *T. rubrum* in twelve culture tubes, *A. nidulans* in three tubes and both species in thirty-seven tubes. *A. nidulans* was isolated from every infected nail, which included both great toe nails and the index, middle and little finger nails of the left hand. Twelve specimens from the uninfected nails of this patient yielded no fungi of any species on culture. The characteristic green discoloration seen in the previously described case was again present in the nails in this second case, along with the usual signs of onychomycosis. A direct examination of numerous specimens of the infected nail plates in a 10 per cent solution of potassium hydroxide always revealed many hyphal elements.

In view of the aforementioned findings we have made an intensive search for other cases of this type during the past six months. Thirteen more cases of aspergillosis of the nail have been observed during this period. In all varying numbers of finger nails and toe nails were involved, a typical green discoloration was present, aspergillus growths were produced on culture, and hyphae or spores were revealed on direct microscopic examination. Six cases were followed completely, and in the other 7 the patients were examined as transient outpatients with no follow-up.

#### METHODS

Specimens of nail tissue were obtained, great care being taken against contamination. The feet were washed well with soap and water, followed by alcohol. The outer layers of the infected nails were then scraped away with a flamed scalpel, the inner brittle, crumbling portion being exposed. The scalpel was again flamed, and pieces of this inner portion were scraped directly into a sterile Petri dish, which was then covered immediately and sent to the laboratory. When received at the laboratory, the specimens were first inoculated into four routine agar slants: Sabouraud's dextrose, corn meal, wort and malt. The remaining particles of the nail were then examined microscopically, after being cleared with a 10 per cent potassium hydroxide solution.

The cultural and the microscopic data on the 6 cases which were followed are given in the table. The cultures of *Aspergillus* and *Trichophyton* obtained in these cases were sent to the Army Medical School in Washington, D. C., for confirmation of species. An additional 7 cases have been observed and the nails treated without complete laboratory follow-up. Primary cultures were made in them, however, with the isolation of *Aspergillus glaucus* in 4 and *A. nidulans* in 3 cases.

Culture of material taken from the nails in these cases presented a picture not found in cases in which there is no infection of the nails but in which accidental contamination has occurred. In a case of true infection all tubes inoculated began to show colonies at the points of inoculation, as many as a dozen small gray colonies appearing on a single slant in about three days. Repeated specimens taken several months apart produce the same cultural picture. This type of multiple colony growth has been found only in the clinically typical cases of ungual infection. Of 1,732 culture tubes of fungous mediums inoculated with specimens of skin and nails during the past sixteen months, only 7 per cent have shown contamination due to *Aspergillus*. On numerous agar plates exposed as

# Results of Microscopic and Cultural Examinations

Case	Date	Potassium Hydroxide Slide	Medium	Species Recovered
1	March 17, 1945	Positive	Sabouraud's	A glaucus
			Corn meal	A glaucus
			Wort agar	A glaucus
			Malt agar	A glaucus
	March 17, 1945		Sabouraud's	A glaucus
			Corn meal	A glaucus
			Wort agar	A glaucus
			Malt agar	A glaucus
	March 27, 1945		Sabouraud's	A glaucus
			Corn meal	A glaucus
			Wort agar	A glaucus
			Malt agar	A glaucus
	March 27, 1945		Sabouraud's	A glaucus
			Corn meal	A glaucus
			Wort agar	A glaucus
			Malt agar	A glaucus
	April 23, 1945		Sabouraud's	A glaucus
			Corn meal	A glaucus
			Wort agar	A glaucus
			Malt agar	A glaucus
	April 23, 1945		Sabouraud's	A glaucus
			Corn meal	A glaucus
			Wort agar	A glaucus
			Malt agar	A glaucus
2	April 12, 1945	Sabouraud's	A glaucus	
		Corn meal	A glaucus	
		Wort agar	A glaucus	
		Malt agar	A glaucus	
	April 20, 1945	Sabouraud's	A glaucus	
		Corn meal	A glaucus	
		Wort agar	A glaucus	
		Malt agar	A glaucus	
	April 20, 1945	Sabouraud's	A glaucus	
		Corn meal	A glaucus	
		Wort agar	A glaucus	
		Malt agar	A glaucus	
3	April 7, 1945	Sabouraud's	A nidulans	
		Corn meal	A nidulans	
		Wort agar	A nidulans	
		Malt agar	A nidulans	
	April 17, 1945	Sabouraud's	A nidulans	
		Corn meal	A nidulans	
		Wort agar	A nidulans	
		Malt agar	A nidulans	
4	April 10, 1945	Sabouraud's	A glaucus	
		Corn meal	A glaucus	
		Wort agar	A glaucus	
		Malt agar	A glaucus	
	April 17, 1945	Sabouraud's	A glaucus	
		Corn meal	A glaucus	
		Wort agar	A glaucus	
		Malt agar	A glaucus	
5	Dec 28, 1944	Sabouraud's	A glaucus and T rubrum	
		Corn meal	A glaucus and T rubrum	
		Wort agar	A glaucus and T rubrum	
		Malt agar	A glaucus and T rubrum	
	April 26, 1945	Sabouraud's	A glaucus and T rubrum	
		Corn meal	A glaucus and T rubrum	
		Wort agar	A glaucus and T rubrum	
		Malt agar	A glaucus and T rubrum	
6	Feb 19, 1945	Sabouraud's	A glaucus and T rubrum	
		Corn meal	A glaucus and T rubrum	
		Wort agar	A glaucus and T rubrum	
		Malt agar	A glaucus and T rubrum	
	March 3, 1945	Sabouraud's	A glaucus and T rubrum	
		Corn meal	A glaucus and T rubrum	
		Wort agar	A glaucus and T rubrum	
		Malt agar	A glaucus and T rubrum	

checks in the laboratory there grew only an occasional colony of *Aspergillus*. In the laboratory fungous contamination has been kept to a minimum by using only tubed mediums as a routine and by forbidding the opening of mature cultures of fungi in the bacteriology section.

#### COMMENT

The clearcut cultural findings in our cases of onychomycosis due to *Aspergillus*, coupled with the gross physical characteristics, leave no doubt that this disease is a clinical entity. We have never observed the typical green discoloration seen in aspergillosis of the nails in any of our cases of proved onychomycosis due to other fungi.



Fig 2—Onychomycosis due to infection with *Aspergillus*

In view of our observations it is our opinion that onychomycosis can be caused primarily by the following species of *Aspergillus*: *A. nidulans*, *A. glaucus* and *A. flavus*. Multiple infection of the nails with one of these species of *Aspergillus* and *T. rubrum* can also occur.

The clinical picture of aspergillosis of the nail is as follows: thickening, brittleness, greenish or yellowish discoloration, vertical striations and crumbling of the distal portions of the infected nail (fig 2). The

treatment in all cases of onychomycosis is highly unsatisfactory at present because avulsion of the nail plates, roentgen ray therapy, application of fungicidal drugs and repeated scraping of the nail have not helped in any of our cases or in others of which we have knowledge. It is hoped that by the light being shed on the cause of onychomycosis new and effective methods of therapy may be developed.

#### SUMMARY

A careful mycologic study of 13 cases of onychomycosis disclosed that *Aspergillus glaucus* or *Aspergillus nidulans* can cause this disease whether present alone or occurring in conjunction with *Trichophyton rubrum*. Repeated cultures in 6 cases disclosed that in 3 the disease was caused by *A. glaucus*, in 1 by *A. nidulans* and in 2 by double infection with *A. glaucus* and *T. rubrum*. Seven additional cases were observed, in which cultures were made once. In these the disease was found to be caused by *A. glaucus* or *A. nidulans*. In the 13 cases there were all the usual characteristics of other forms of fungous infection of the nail in addition to a typical greenish discoloration of the nail plate. Evidence is presented to show that the species of *Aspergillus* culture in these cases cannot be considered accidental clinical or laboratory contaminations but were actually present in the infected nails in considerable quantity. It is therefore postulated that the nails of the fingers or the toes of human beings may be invaded by some species of *Aspergillus*, with production of a pathologic condition resembling the onychomycoses produced by other fungi.

2426 Eutaw Place, Baltimore  
Coral Gables, Fla

# DERMATOPHYTOSIS DUE TO COMBINED INFECTION WITH TRICHOPHYTON INTERDIGITALE AND TRICHOPHYTON PURPUREUM

Report of a Case

EMANUEL MUSKATBLIT, M D

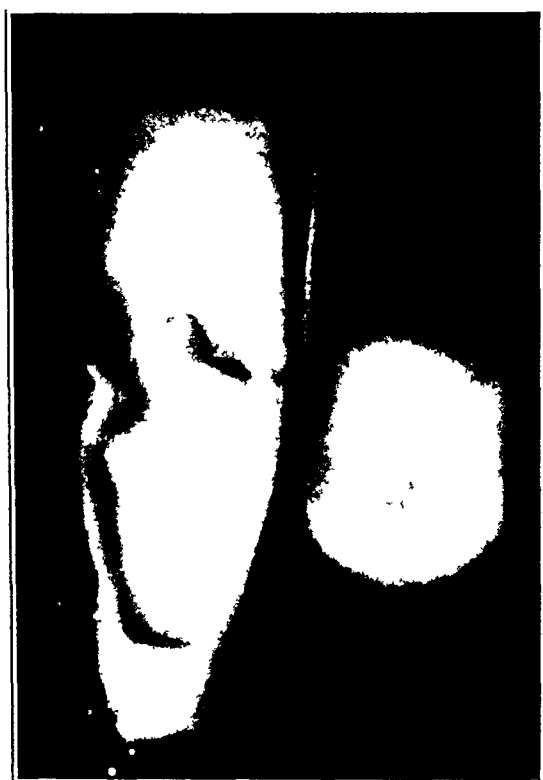
NEW YORK

A WHITE woman aged 42 gave a history of an itchy eruption of four months' duration on the left foot, which was rapidly followed by an eruption on each hand. The examination revealed minute deep-seated intraepidermal vesicles on the fingers of both hands and on the left palm, without a noticeable inflammatory reaction. On the left sole there was a vesicular eruption, with erythema and scaling. Scrapings from the fingers revealed no fungi in a potassium hydroxide preparation, scrapings from the left sole showed fungous filaments and chains of spores. This was, therefore, a case of dermatophytosis of the left sole. The eruption on the hands could be considered a dermatophytid because of its clinical features and the lack of contact with possible cutaneous irritants. Cultures made on Sabouraud's medium (dextrose-peptone-agar) with material taken from the left sole produced a curious combination of colonies of two different types, growing side by side in the same culture tubes. The one, identified as a colony of *Trichophyton interdigitale*, was white and downy, with irregular grooves, folds and convolutions. The other, identified as a colony of *Trichophyton purpureum*, showed an elevated center covered with pinkish down, a flat, yellow and powdery middle zone and a peripheral fringe of submerged rays, powdery on the surface and deep red on transillumination. Later on this culture was completely covered with a pink down. Culture mounts of both fungi presented identical forms of sporulation, namely, numerous small conidia (aleurospores) on simple and branched filaments and chlamydoconidia. Neither spiral coils nor fusiform structures were found. The identification of the two different species was based on different gross appearance, especially on the presence of red pigment in the surface down and in the basal layer of colonies classified as *T. purpureum*. In treatment a 5 per cent solution of salicylic acid in alcohol was applied on the foot once daily and a zinc oxide-talcum lotion on the hands. Four fractional doses of roentgen rays (75 r) were also given at weekly intervals. Four months later the patient was free from any symptoms or signs of her disease. Scrapings from the left sole yielded no fungi.

This case is interesting not only as a mycologic curiosity with two different fungi on cultures. Both species, *T. interdigitale* and *T. purpureum*, were isolated from a vesicular eruption. *T. purpureum* usually causes dry, scaly, infiltrated and lichenified lesions. *T. interdigitale* often produces vesicular eruptions. This case presented clinical features common for *T. interdigitale*. The other partner of this fungous symbiosis, *T. purpureum*, did not show its clinical characteristics. The same was true in regard to the results of the therapy. Lesions pro-

duced by *T. purpureum* are noted for their resistance to treatment. In this case a mild type of treatment cleared the eruption clinically and microscopically. The presence of an eruption on the hands typical for a dermatophytid is a feature common in diseases due to *T. interdigitale* and practically unknown in *T. purpureum* infections.

It is possible that *T. interdigitale* acted as an antagonist of *T. purpureum* and inhibited the latter's vitality. It is also possible that *T. interdigitale* stimulated the immunologic response of the skin and thereby contributed to the cure. *T. purpureum* is known as a poor



*Trichophyton interdigitale* (left) and *Trichophyton purpureum* (right) isolated from a case of dermatophytosis of the foot

sensitizer, a fact which explains at least partially the poor therapeutic results. Whatever the cause, it was a symbiosis of two pathogenic fungi in which one of them played the predominant part, determining the clinical picture and the course of the disease, while the other behaved more like an innocuous saprophyte.

The interesting question whether an artificial inoculation of *T. interdigitale* into the skin of a patient with lesions due to *T. purpureum* will increase the immunologic response and speed up the cure can be answered only by experimentation.

55 West Forty-Second Street

# ERYTHEMA MULTIFORME AND ERYTHEMA NODOSUM

A Comparative Study of Fifty-Four Patients

RAY O. NOOJIN, M.D.

BIRMINGHAM, ALA.

AND

J. LAMAR CALLAWAY, M.D.

DURHAM, N. C.

NOT ALL the etiologic factors involved in the causation of erythema multiforme are as yet clear. It is also true that in the therapeutics of this dermatosis success is occasionally difficult to obtain. Because of these facts, an analytic study was made of 40 unselected patients having typical erythema multiforme exudativum. Six of these patients had accompanying bullous lesions. In view of the close relationship between erythema multiforme and erythema nodosum, 14 additional patients with the latter disease were also studied for comparison. Examples of both types of lesions were not exhibited by any one patient in this study.

The 54 patients were examined carefully, and every attempt was made to evaluate thoroughly the background, the history, the physical findings and the accessory clinical findings in each patient. In addition to inquiry being directed to age, sex, race, temperature, systemic symptoms, family history, season of incidence, occupation, duration of disease and characteristics of lesions, special attention was paid to foci of infection, laboratory findings in the peripheral blood, urinalyses, roentgenograms, condition of the nose and the throat, bacteriologic cultures, intradermal tests, presence or absence of nervous tension and response to various types of therapy.

In table 1 are listed the average age of the patients, their distribution as regards sex and the duration of the lesions in both groups. It is significant that among the 54 unselected members of the two erythema groups not one was a Negro, although there is seen 1 Negro patient for every 3 white patients in the medical clinics of Duke Hospital. The known greater frequency of occurrence of erythema nodosum in females is substantiated, whereas in patients with erythema multiforme the sexes tend to be more evenly represented. In adults the age of incidence, although variable, was most commonly the fourth decade. No patients of pediatric age were included in this study. Most of the patients had their disease less than four weeks.

From the Division of Dermatology and Syphilology of the Department of Medicine, Duke University School of Medicine, Durham, N. C.

Certain factors were found to be inconsistent and apparently of little significance with reference to etiologic considerations, namely occupation and family and past histories, with particular emphasis being given to tuberculosis, allergic diseases, nervous tension or other familial influences

Table 2 demonstrates the tendency of the incidence to increase during the spring and fall seasons, which has long been recognized.<sup>1</sup> It would seem difficult to appreciate this definite seasonal variation unless one could assume that it is closely related to other factors

TABLE 1—Average Age, Race and Sex of Patients and Duration of Lesions

Disease	No of Patients	Average Age	Race		Sex		Duration of Lesion		
			White	Negro	Male	Female	1 Mo	6 Mo	1 Yr
Erythema multiforme	40	39	40	0	21	19	37	2	1
Erythema nodosum	14	30	14	0	3	11	10	1	0

Guy<sup>11</sup> originally reported an epidemic of erythema multiforme occurring during February and March 1918 in 47 patients. Hemolytic streptococci were isolated in cultures of material from either the throat or the vaccination wounds of 32 of these patients. In addition, 9 patients harbored pyogenic streptococci in their throats. Spink<sup>12</sup> has pointed out the similarity between the curves of incidence of erythema nodosum and known streptococcic infection in 95 patients with acute follicular tonsillitis, from each of whom beta hemolytic streptococci

TABLE 2—Monthly Incidence of Erythema Multiforme and Erythema Nodosum

Disease	No of Patients	Jan	Feb	March	April	May	June	July	Aug	Sept	Oct	Nov	Dec
Erythema multiforme	40	1	7	3	6	4	0	2	4	1	6	4	0
Erythema nodosum	14	3	1	1	2	3	2	0	1	0	1	0	0

were isolated. The seasonal incidence of the common cold as determined by Kler,<sup>2</sup> however, does not coincide precisely with the seasonal occurrence of erythema multiforme and erythema nodosum. Thus, the possible relationship between common infections of the upper part of the respiratory tract and these two erythemas warrants further study.

1 (a) Guy, W. H. Erythema Multiforme. A Clinical and Laboratory Study of Forty-Seven Cases, J. A. M. A. **71** 1993 (Dec 14) 1918. (b) Spink, W. W. Pathogenesis of Erythema Nodosum, with Special Reference to Tuberculosis, Streptococcic Infection and Rheumatic Fever, Arch. Int. Med. **59** 65 (Jan) 1937.

2 Kler, J. H. An Analysis of Colds in Industry, Arch. Otolaryng. **41** 395 (June) 1945.



The systemic signs and symptoms which accompany erythema multiforme and erythema nodosum emphasize the systemic nature of the two diseases. Table 3 lists the more commonly occurring systemic signs and symptoms in the order of their frequency. Fever and generalized malaise were most often present.

In table 4 are listed the average results of numerous laboratory determinations in both groups. The normality of the color indexes and

TABLE 3—Common Noncutaneous Signs and Symptoms of Erythema Multiforme and Erythema Nodosum

Disease	No of Patients	Fever	Malaise	Cough	Arthralgia	Nausea and Emesis
Erythema multiforme	40	14	8	8	5	2
Erythema nodosum	14	7	6	3	5	2

of the differential leukocyte counts is apparent. The slightly lower hemoglobin determinations of the erythema nodosum group may have been due to the fact that most of these patients were women. Corrected sedimentation rates were consistently elevated above the upper limit of normal. Slightly elevated leukocyte counts were usually present,

TABLE 4—Average Accessory Clinical Determinations in Cases of Erythema Multiforme and Erythema Nodosum

	Disease	
	Erythema Multiforme	Erythema Nodosum
Number of patients	40	14
Hemoglobin, Gm (Sahl)	13.6	12.4
Color index	0.98	0.95
Corrected sedimentation rate	28	26
Wetmann coagulation band (normal 6)	4	5
Leukocyte count	10,070	11,870
Differential leukocyte count	Per Cent	Per Cent
Polymorphonuclears		
Segmented forms	65	65
Stab forms	5	5
Juvenile forms	1	1
Basophils	1	0
Eosinophils	3	1
Monocytes	5	6
Large lymphocytes	7	3
Small lymphocytes	15	19

and only one count was below 5,000. Consistent eosinophilia was not a feature. The Wetmann coagulation band averaged 4 in the erythema multiforme group and 5 in the erythema nodosum group, indicating that in both instances exudative pathologic processes were present.<sup>3</sup>

3 Dees, S. C. The Wetmann Reaction in Bronchial Asthma, J. Allergy 14:469 (Sept.) 1943.

A decided effort was made to check each patient for foci of infection, and it was interesting to find that 45 of the 54 patients had definite evidences of infection. It is recognized that the significance of this observation is open to question. As shown in table 5, the roentgenologic evidences of infection were found frequently to involve, in the order named, the chest, the sinuses and the teeth. Kerley<sup>4</sup> found evidence of recent intrathoracic disease by roentgenologic examination in 28 of 37 patients with erythema nodosum. The average age in his group was 21 years. This lower average age may possibly account for the greater

TABLE 5—*Incidence of Infection in Patients with Erythema Multiforme and Erythema Nodosum as Demonstrated by Roentgenologic and Otolaryngologic Study*

Disease	Otolaryngologic Examination			Roentgenologic Examination					
				Sinus		Chest		Teeth	
	Tonsil litis	Sinu sitis	Normal	Infec tion Present	Normal	Infec tion Present	Normal	Infec tion Present	Normal
Erythema multiforme	8	7	1	7	22	11	24	6	17
Erythema nodosum	6	1	1	1	9	5	8	1	4

TABLE 6—*Incidence of Cultured Organisms in Patients with Erythema Multiforme and Erythema Nodosum*

	Disease	
	Erythema Multiforme	Erythema Nodosum
Cultures of material from nose and throat or of sputum		
Str viridans	15	6
Str pyogenes	1	0
Staph aureus (hemolytic)	9	0
Staph aureus	3	1
Negative	6	1
Cultures of stool		
Hemolytic organisms	7	1
Negative	0	0
Cultures of urine		
Staph aureus	2	2
Negative	3	1

incidence of recent pulmonary disease in his group. An examination by an otolaryngologist also revealed in some patients tonsillitis, pharyngitis or sinusitis. The figures are also shown in table 5. All patients who appeared on routine examination to have probable disease of the upper part of the respiratory tract were referred to an otolaryngologist.

Table 6 discloses the types of organisms isolated from the nose and the throat and from the sputum, the urine and the stools. Alpha hemolytic streptococci (*Streptococcus viridans*) were found to be present most frequently.

<sup>4</sup> Kerley, P. The Etiology of Erythema Nodosum, *Brit J Radiol* **16** 199 (July) 1943.

Of 17 female patients who had pelvic examinations, 8 were found to have chronic cervicitis or evidence of other pelvic inflammatory disease. Four of these 8 patients had erythema nodosum and 4 had erythema multiforme.

Of 9 patients without obvious evidence of infection, only 1 gave a history of possible drug sensitivity and of taking the suspected drug prior to the outbreak of his cutaneous eruption. This particular patient was the only one, in the entire number of 54 patients, who by history could fairly definitely be said to have a dermal reaction probably attributable to drug sensitivity. Only 18 of the 54 patients gave a history of taking any drug during the four weeks prior to the onset of their disease. Ten of the 18 patients had been taking one of the sulfonamide compounds, and the other patients had been taking proprietary preparations. Of the 10 patients receiving sulfonamide compounds prior to the study, 2 again were given sulfonamide drugs without exacerbation of their eruption. By history, one suspects that drugs played an insignificant causative role in the eruptions of these 54 patients.

Five of 12 patients were sensitive to staphylococcus toxoid by intradermal testing. Similarly, 6 of 15 patients were sensitive to one or more of the streptococcic allergens. Ten patients were tested intradermally with the various food allergens and pollens. In 4 of these the tests elicited no reactions at all, whereas in the remaining 6 the tests elicited one or more positive reactions. These results, however, could not be correlated by history with the cause of the disease.

Of 8 patients with erythema multiforme in whom studies of vitamin levels were undertaken, all were found to have adequate plasma levels of vitamins C and A and carotene.<sup>5</sup>

The average patient was free of his disease within four weeks after the onset, apparently regardless of the nature of the therapy administered. Definitely, those patients with erythema nodosum, which involved most commonly and most intensively the lower extremities, responded much more rapidly when they were put to bed with their legs elevated. Generally the same can be said for rest in bed as regards the patients with erythema multiforme.

Of 40 patients with erythema multiforme, all but 2 were hospitalized for investigation and treatment. Of the 38 patients hospitalized, 36 (95 per cent) were well within four weeks from the time of the onset of their disease and had no recurrences for at least six months after their recovery. Their treatment could be divided essentially into two types: (1) medical (28 patients), which included the administration of one or any combination of salicylates, sulfonamide compounds, penicillin vaccine (for desensitization) or roentgen rays, (2) primarily

<sup>5</sup> Callaway, J. L., Milam, D. F., and Noojin, R. O. Nutritional Survey of 354 Dermatologic Patients, *Arch. Dermat. & Syph.* **51**: 266 (April) 1945.

surgical (10 patients), which included tonsillectomy and adenoidectomy or removal of abscessed teeth. Regardless of whether the patient was treated in the hospital primarily medically or surgically, the average patient became well in less than four weeks from the time of the onset of his disease.

The erythema nodosum group responded similarly. Rest in bed, with elevation of the lower extremities, was noted significantly to be desirable for patients with erythema nodosum who had lesions on their lower extremities. In 1 patient frank pulmonary tuberculosis developed within eight months after the onset of erythema nodosum. At the time the erythema nodosum was present, a roentgen film showed the chest was normal.

#### SUMMARY AND CONCLUSIONS

An analytic and comparative study has been made of 40 patients with erythema multiforme and 14 patients with erythema nodosum.

Both diseases appear to be less common among Negroes.

Except for the clinical appearance, the sex incidence and the possible relationship of tuberculosis, erythema multiforme and erythema nodosum are remarkably alike in many of their manifestations.

The fourth decade held the largest adult age group for both diseases.

Fever and generalized malaise most often accompanied the cutaneous manifestations.

Laboratory examination disclosed consistently a normal color index, a normal differential leukocyte count without eosinophilia, an elevated sedimentation rate, a slightly elevated total peripheral blood leukocyte count and a Weltmann coagulation band of less than 6.

Forty-five of the 54 patients had one or more evidences of focal infection.

A streptococcus was isolated from these patients more frequently than any other organism.

Drug sensitivity apparently was of little significance in either group in the causation of disease.

Intradermal tests in general did not significantly contribute to the management of either disease.

Most patients were free of their disease within four weeks of the onset, regardless of the nature of the therapy administered.

Mrs. Jane Stitt and Mrs. Judy Gadsden gave helpful assistance in the collection and the analysis of the material presented.

## Clinical Notes

### PROGRESSIVE SYPHILITIC OPTIC ATROPHY BENEFITED BY COMBINED PENICILLIN AND FEVER THERAPY

#### Report of a Case

JOSEPH L FETTERMAN, M D ,

In Collaboration with J H BARR, M D  
CLEVELAND

THE DRAMATIC improvement in vision achieved by the combined use of penicillin and fever therapy in a case of advancing syphilitic optic atrophy prompts this report

S M, a white man aged 34, noticed dimness of vision in the left eye late in November 1944. At the beginning, this blurring was inconstant and limited to "the inside, near my nose." Gradually this disturbance became constant and more extensive until, finally, all the vision was gone. When the patient consulted Dr W E Bruner in January 1945, there was total blindness of the left eye. Dr Bruner found pallor of the nerve head on the left side and also Argyll-Robertson pupils.

S M was referred to me by Dr Bruner and was examined on Feb 1, 1945. At the initial visit he had total blindness in the left eye and rather casually mentioned some visual difficulty with the right eye as well. Every so often a watery film seemed to cover objects at which he looked. Examination showed myotic pupils which did not react to light but did constrict on accommodation. The left disk was pale white and its margins sharply circumscribed. The right disk was slightly pale.

Except for the eyes, all the functions of the cranial nerve were intact. The results of neuromuscular examination and the sensory tests were normal. Mentally, the patient was of average intelligence, his emotional state was normal and he was cooperative in every way. Unusual was his apparent indifference to the failing vision and his delay in seeking help. As regards past history, he mentioned that at the age of 15 he had a penile lesion, which was treated locally and then neglected.

S M was placed in the University Hospitals for further study and treatment. The Kline reaction of the blood was positive. The spinal fluid was under normal pressure, the cell count revealed 33 lymphocytes, the total protein level was 28.5 mg per hundred cubic centimeters and the Wassermann reaction was positive in dilutions of 0.5 and 1 cc. The colloidal gum mastic curve was 3322100000. Results of the remainder of the laboratory tests and the physical examination were normal.

At the time of hospitalization, visual field studies showed a slight constriction in the right field. There had been additional loss of visual acuity since the initial examination in my office. The patient voluntarily stated that he could no longer read the comics but was still able to read the headlines of the daily newspaper.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Western Reserve University School of Medicine.

Even the reading of large print required determined effort, and the page seemed blurred by a watery sheen. At this time the disk was more pale than several days previously.

Because of the rapidly advancing optic atrophy, fever therapy was started immediately, typhoid vaccine being used intravenously while the spontaneous paroxysms from a malarial inoculation were awaited. The patient was allowed to have eleven paroxysms in all, seven with typhoid vaccine and four with malaria, for a total of forty-four and a half hours, above 40 C (104 F). Simultaneously with fever therapy, penicillin was administered. The patient was given 25,000 units of penicillin intramuscularly every three hours, for a total of 4,000,000 units in twenty days.

At the end of the first week, during which he had several chills and was given over 1,000,000 units of penicillin, the patient stated that he could see more clearly. He could now read the headlines of the newspaper more readily. There was additional improvement during the second week. When the treatment was completed, the patient was able to read the fine print of his favorite comic page and the watery sheen was gone.

S. M. was discharged early in March 1945, and his progress was followed thereafter. In the middle of March, the vision was tested with the rating reading card of the American Medical Association. The patient was able to read with his right eye the smaller letters at a distance of 14 inches (35.5 cm), the rating being 56.5 per cent of normal. Toward the end of March, he was able to read the finest print, with a rating of 100 per cent. However, the color of the disk was still distinctly pale. Throughout the period of observation, the left eye remained totally blind and the disk white.

Early in April, the patient resumed his occupation as a machinist and was able to handle his tools skilfully. At this time he could see perfectly well out of the right eye and could read the finest print as long as he wished, without any fatigue. Acuity for near and distant vision was roughly normal. A reexamination in June 1945 (one hundred and nine days after onset of therapy) revealed satisfactory vision in the right eye and improvement in the spinal fluid. The colloidal gum mastic curve was normal, the Wassermann reaction with 0.1 cc was negative, with 0.5 cc 4 plus and with 1 cc 4 plus, the cell count was 2 lymphocytes, and the total protein level was 34 mg per hundred cubic centimeters.

#### COMMENT

Syphilitic optic atrophy is one of the most serious manifestations of syphilis. In my experience, when the vision in one eye is gone and in the other is dim, the course is usually a downward one. Moore<sup>1</sup> stressed the poor prognosis in any patient with loss of vision in one eye and progressive changes in the other. Consequently, physicians who saw S. M. on his admission to the hospital had a feeling of hopelessness. For this reason it was decided not to rely on fever therapy alone but to use penicillin also. This decision to use penicillin depended on its proved success in treatment of early syphilis. There is a favorable clinical report by Stokes and colleagues,<sup>2</sup> who had had good results with penicillin in cases of ocular

1 Moore, J. E., Kemp, J. E., and others. *The Modern Treatment of Syphilis*, ed. 2, Springfield, Ill., Charles C. Thomas, Publisher, 1941.

2 Stokes, J. H., Sternberg, T. H., Schwartz, W. H., Mahoney, J. F., Moore, J. E., and Woods, W. B., Jr. *The Action of Penicillin in Late Syphilis*, *I. A. M. A.* **126**: 73 (Sept. 9) 1944.

syphilis "In ocular syphilis, simple inflammatory processes respond, later and more complicated lesions such as the optic neuritides and interstitial keratitis recover, relapse, present resistance and residues proportional to damage already done"

The therapeutic result obtained in the case reported was distinctly superior to the improvement in several cases reported by Stokes and his co-workers<sup>3</sup> in which penicillin alone was used. These investigators concluded "Penicillin alone may favorably affect any type of active neurosyphilis, symptomatic and asymptomatic. It may arrest progression in primary optic atrophy with short observation, has thus far blinded no one, may produce slight improvement in vision and fields, may return the spinal fluid to normal, including Type III, may fail (in lower dosage) to stop a localized chiasm lesion, despite such spinal fluid improvement"

#### SUMMARY

A case of syphilitic optic atrophy is reported in which there was total blindness in one eye and progressive loss of vision in the other eye, with pallor of the nerve head. Treatment with combined fever and penicillin was instituted. The condition of the blind eye remained unchanged, but almost normal vision was restored to the other eye. However, eighteen months after the apparent recovery, the visual acuity decreased. Further treatment has been instituted.

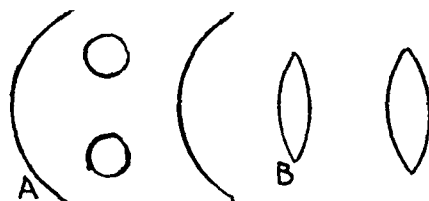
Dr W E Bruner and Dr A B Bruner checked the patient's visual status from time to time, and the Department of Dermatology and Syphilology, Dr H N Cole, Director, furnished the penicillin and the dosage outlined.

3 Stokes, J H, and others. Penicillin in Late Syphilis, *Am J Syph, Gonorr & Ven Dis* 29 313 (May) 1945

#### BIOPSY GUIDE

ROBERT P LITTLE, M D, NEW YORK

The removal of a specimen for biopsy may be facilitated by the use of a flat metal guide, convex on one border and concave on the other. The first incision may be made along the convex border to the desired extent and the ellipse



A, guide, B, incisions of two sizes

completed by turning the guide and cutting along the concave border. If it is preferred, the concave border may be used for both incisions.

## Correspondence

### DOSAGE IN TOPICAL THERAPY

*To the Editor* —The report of Dr Herman Goodman in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, July 1946, page 62, is highly provocative in that it brings into sharp focus our understanding of dosage in topical therapy for the skin. Essentially, the establishment of effective dosage of an active drug involves maintenance of a proper concentration of the drug in the tissue concerned. And so, for internal therapy, dosage is based on body weight, and exhibition of the drug is repeated at proper intervals to keep adequate its concentration in the organism over the required period. For topical treatment the same principles operate except that surface area is substituted for body weight in estimating the anticipated concentration of the drug in skin, for the skin covered by the medication is accepted as the only area of skin receiving therapy.

Vehicles for topical drugs serve the purpose, among others, of making possible the even distribution of the drug over the whole unit of cutaneous area treated. Thus, if it is assumed that 1 Gm of a grease base mixture is to be spread over 4 square inches (25.8 sq cm) of skin, a 1 per cent salve of salicylic acid in this vehicle would supply 10 mg of the acid evenly dispersed over these 4 square inches. No matter what the character of the vehicle, if 1 Gm of the medicated salve contained 10 mg of drug and the vehicle permits a spreading of the drug evenly over the 4 square inches, the dosage offered the skin remains identical, independent of what happens to the vehicle thereafter (evaporation from the cutaneous surface, etc.)

Dr Goodman does not believe that this is so. His explanation as to why this is not so reveals an unusual understanding of topical dosage.

To quote Dr Goodman

"Chrysarobin is prescribed in a medium of chloroform prescriptions disclose great variation in the percentage of chrysarobin ordered. The evaporation of the chloroform from the skin at the time of application levels all distinction as to percentage of chrysarobin. The film on the skin is 100 per cent chrysarobin."

Levels all distinction indeed! Yes, the film on the skin is 100 per cent chrysarobin but 1 cc of a 1 per cent solution is 10 mg of film of chrysarobin, 1 cc of a 5 per cent solution is 50 mg of film of chrysarobin, both are 100 per cent films of chrysarobin, but what of the quantity of drug in each film?

HERMAN SHARLIT, M D, New York



## Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

LYMPHOGRANULOMA VENEREUM F C COMBES, O CANIZARES and S LANDY,  
Am J Syph, Gonorr & Ven Dis **29** 611 (Nov) 1945

The authors report on the result of the formaldehyde-gel test and the serum albumin-globulin ratio as determined in 42 cases of lymphogranuloma venereum. In 38, or 90.5 per cent, the result of the test was positive and the serum showed hyperglobulinemia. In 15 cases, followed for a period of sixteen weeks, there was a decided tendency for the result of the test to return to normal after clinical cure.

The formaldehyde-gel test is a simple reliable bedside procedure by which to determine the presence of hyperglobulinemia in patients with lymphogranuloma venereum. The result of this test and the albumin-globulin ratio should be used as aids in treatment and as indications of biologic cure in all cases of lymphogranuloma venereum.

STUDIES ON CHANCROID PAUL B BEESON and ALBERT HEYMAN, Am J Syph,  
Gonorr & Ven Dis **29** 633 (Nov) 1945

Because culture of material taken from a lesion suspected to contain the Ducrey bacillus as a means of diagnosis of chancroid has generally been abandoned as impracticable, the authors report in detail the technical method which has given them the best results. While an exact statement of the efficiency of diagnosis by culture could not be made, it seemed probable that a diagnosis can be made by culture in at least 75 per cent of all cases of chancroid. In pure culture the Ducrey bacillus grows well on mediums containing a body fluid, such as blood or serum. The medium which gave the best results was defibrinated rabbit blood. A technical detail of importance is the use of a very small inoculum from the genital lesion. The morphologic aspects and the staining of the Ducrey bacillus are sufficiently characteristic to permit a reasonably certain diagnosis based only on an examination of stained smears from the rabbit blood cultures.

CARDIOLIPIN ANTIGENS IN THE SERODIAGNOSIS OF SYPHILIS CHARLES R REIN  
and HILFRED N BOSSAK, Am J Syph, Gonorr & Ven Dis **30** 40 (Jan)  
1946

Cardiolipin antigen, composed of cardiolipin (0.2 per cent), a substance isolated from beef heart, and lecithin (1.3 per cent), was successfully adapted for use in a microflocculation slide test for syphilis. The sensitivity of the microflocculation slide test made with this antigen was higher than that observed with Kline diagnostic, Mazzini, Kahn and Kolmer tests performed in the authors' laboratory. The cardiolipin antigen showed extraordinary specificity in the presence of malarial infection. Such specificity was not evident when the serums tested were from patients with leprosy and infectious mononucleosis.

THE RELATIVE PROPHYLACTIC EFFECTIVENESS AGAINST SYPHILIS OF OINTMENTS  
CONTAINING CALOMEL IN DIFFERENT PARTICLE SIZE WILLIAM L FLEMING  
and MARY H WOLF, Am J Syph, Gonorr & Ven Dis **30** 47 (Jan) 1946

The authors carried out an experiment with rabbits to evaluate the effect of the particle size of mild mercurous chloride on the efficacy of ointment of mild mercurous chloride as used in prophylaxis of syphilis. Three different ointments

containing mild mercurous chloride in 100 micron, 5 micron and 1 micron particle size were used

Much greater protection was obtained with the ointments containing the smaller particles, that containing the 100 micron particles being relatively ineffective. The amount of ointment used seemed to play little part in the results, although the larger dose did afford somewhat better protection than the smaller. The results also seemed to give some indication that the local action of mild mercurous chloride was more important than the systemic.

**SYPHILITIC VASCULAR OR CARDIOVASCULAR DISEASE OCCURRING IN EARLY ADULT LIFE FOLLOWING ACQUIRED SYPHILITIC INFECTION** I L SCHAMBERG, *Am J Syph, Gonorr & Ven Dis* 30 58 (Jan) 1946

Five patients were presented, in whom serious syphilitic lesions of the vascular or cardiovascular organs developed in early adult life. In 3 the interval between the early lesions of syphilis and the first symptoms of vascular disease was two, thirteen and fifteen years, respectively. No conclusions could be drawn as to what effect the age at which syphilis is acquired has on the rapidity of progression of syphilitic vascular disease.

**STUDIES ON LIVER FUNCTION** EWART HINDS and FREDERICK KATZ, *Am J Syph, Gonorr & Ven Dis* 30 70 (Jan) 1946

Greatly impaired hepatic function and significantly reduced prothrombin concentration indicate arsenical toxicity. In such cases therapy should be stopped at once. Two fatal cases of toxic encephalopathy are reported. In 1 case death occurred after a total dose of 240 mg of *oxyphenarsine hydrochloride* (mapharsen). In the other case death occurred after a total dose of 720 mg of the drug had been given. Because of the inability to predict or to prevent arsenical encephalopathy and because in some patients small doses of arsenicals cause fatal reactions and discontinuation of arsenotherapy does not necessarily prevent the development of serious and sometimes fatal sequelae, the authors feel that massive arsenotherapy should be abolished.

REUTER, Milwaukee

**REVERSAL OF LINGUAL ATROPHIC CHANGES WITH NICOTINAMIDE THERAPY** ELMER L SEVRINGHAUS and EMMA D KYHOS, *Arch Int Med* 76 31 (July) 1945

As evidence of nicotinic acid deficiency Kruse described lingual fissures, atrophy of filiform papillae and dental scalloping of the margin of the tongue. Sevringhaus and Kyhos found such changes in 30 of 102 prison inmates. Of 17 men with fissured tongues 14 made significant improvement after taking 50 mg of nicotinamide daily for not more than nineteen weeks. Five men received treatment because of marginal changes, which responded in 3 instances. It was found difficult to gauge improvement in the condition of the papillae, but the authors were satisfied that these changes responded better than did the others. It is concluded that the criteria of chronic aniacinamidosis proposed by Kruse are valid.

Similar changes were noted in 3 anemic patients, whose conditions likewise improved promptly.

**ESOPHAGEAL LESIONS ASSOCIATED WITH ACROSCLEROSIS AND SCLERODERMA** ARTHUR M OLSEN, PAUL A O'LEARY and B R KIRKLIN, *Arch Int Med* 76 189 (Oct) 1945

After reviewing previous reports of 32 cases in which scleroderma was accompanied with esophageal lesions, Olsen, O'Leary and Kirklin analyzed the records of 350 patients with scleroderma or acrosclerosis, after finding dysphagia or esophageal lesions in 36. Their study is concerned chiefly with 18 cases in which conclusive roentgenographic or endoscopic observations were made. In all these cases the symptoms of Raynaud's syndrome preceded or were coincident with

the development of cutaneous manifestations (In 15 of the remaining 18 cases the diagnosis was also acrosclerosis) The cases are reported individually, and the roentgenologic and endoscopic changes are described in detail

The vasomotor phenomena and, in most instances, the sclerodermatous changes preceded the dysphagia or substernal burning, and the esophageal disturbance was most often a delayed manifestation of the disease The authors state that when the esophageal difficulties are obstructive, temporary relief can be obtained almost invariably by dilation of the esophagus with sounds over a previously swallowed thread In cases of cardiospasm associated with acrosclerosis or scleroderma, hydrostatic dilatation is not advisable Sometimes the passage of the esophagoscope alone is enough to relieve the dysphagia It is not advisable to use sounds larger than the no 45 French sound in dilating organic lesions of the esophagus Frequently, a repeated passage of sounds is necessary to maintain an adequate esophageal lumen

CANCER IN RELATION TO USAGES THREE NEW TYPES IN INDIA V R KHANOLKAR and B SURYABAI, Arch Path **40** 351 (Nov-Dec) 1945

The authors had occasion to study, in different parts of India, three types of cancer which they believe may be attributed to certain usages prevalent in those regions In 9 cases of "dhoti cancer" there was squamous cell cancer of the trunk, and the location was along the lines of the greatest friction or pressure of the garment (dhoti) The nature of the garment is such that it subjects to the greatest friction those sites of the body which are often soiled with dust and sweat and have the least opportunity of a thorough cleansing

In certain provinces the natives habitually smoke a local type of cigar, called the chutta, with its burning end inside the mouth Leukoplakic lesions of the hard palate were frequently observed among chutta smokers There is frequent super-vention of carcinoma of a serious type The increased incidence is indicated by the fact that in one province palatal carcinoma was almost six times as frequent as carcinoma of the tongue

Khami, a mixture of a powder of dried tobacco leaf with lime, is deposited in the groove between the front teeth and the lower lip It is left there until it is gradually diluted with saliva and is then swallowed This procedure appears to result frequently in carcinoma of the mouth

In the first and second instances the authors discuss the histologic changes of the carcinoma and the apparently precancerous processes The implications are also thoroughly discussed

LYNCH, St Paul

THE EFFECT OF VIVAX MALARIA ON SPINAL FLUID AND BLOOD SEROLOGIC TEST FOR SYPHILIS HARRY M ROBINSON JR and WILLIAM W MCKINNEY, J A M A **129** 544 (Oct 20) 1945

Serologic tests of the blood and examinations of the spinal fluid were made for 100 nonsyphilitic white men with malaria caused by plasmodium vivax No change had occurred in the Kahn reaction of the spinal fluid of any of these patients There were 33 per cent positive Kahn reactions of the blood and 11 per cent doubtful reactions The serologic reaction for syphilis was negative in all cases at the end of eleven weeks

DIAGNOSIS OF CHANCROID ALBERT HEYMAN, PAUL B BEESON and WALTER H SHEDDON, J A M A **129** 935 (Dec 1) 1945

Biopsy was performed in 59 of the 125 cases in this series, in which the patients were suspected of having either chancroid or venereal lymphogranuloma A histologic diagnosis of chancroid was made in 45 cases In 35 of these the diagnosis of chancroid was confirmed by cultures positive for Ducrey's bacillus

On examination of the sections the lesion is found to consist of three zones The surface zone, or base of the ulcer, is rather shallow and is made up of polymorpho-nuclear leukocytes, fibrin, red blood cells and necrotic tissue Below this is a

fairly wide layer of edematous tissue, in which endothelial cells in various stages of proliferation outnumber all other cellular components. Newly formed blood vessels are numerous and may show palisading with occasional degeneration of the vessel walls and thrombosis. Finally there is a deep zone, which is densely infiltrated by plasma cells and lymphocytes.

Biopsy is limited to cases in which there are primary genital lesions, it is undesirable in patients with small lesions because of the pain involved. Cultural demonstration of the Ducrey bacillus can be accomplished in at least 75 per cent of all cases. Diagnosis by direct smears of material from the genital lesions is possible in approximately 50 per cent of the cases. Autoinoculation does not take with sufficient frequency to make it of value in routine work. The cutaneous test for chancroid is of limited value as an adjuvant to other procedures. In this group of 60 cases in which chancroid was the proved diagnosis positive reactions to cutaneous tests were found in only 46. A positive reaction persists for many years after an infection and therefore may not be significant in reference to the present illness.

ELECTROENCEPHALOGRAPHIC FINDINGS IN CENTRAL NERVOUS SYSTEM SYPHILIS BEFORE AND AFTER TREATMENT WITH PENICILLIN J LAMAR CALLAWAY, HANS LOWENBACH, RAY O NOOJIN, BEATRICE H KUHN and KATHLEEN A RILEY, J A M A **129** 938 (Dec 1) 1945

No correlation exists between the degree of abnormality of the electroencephalographic pattern and the type, the severity or the duration of neurosyphilis. In the majority of cases a definitely but nonspecifically abnormal pattern or a pattern on the borderline between normal and abnormal is found. Thirty-eight patients suffering from neurosyphilis were studied before and after treatment with penicillin. Many whose former electroencephalograms showed abnormal patterns now have electroencephalograms in which the patterns are normal, and the records of most of the remaining ones show varying degrees of improvement. Abnormalities of the electroencephalographic patterns are interpreted as the expression of local cerebral anoxia and a generalized or localized cerebral inflammation.

PENICILLIN FOR ULCERS OF LEG TREATED BY PINCH GRAFTS RUBEN NOMLAND and EVELYN G WALLACE, J A M A **130** 563 (March 2) 1946

A series of 9 cases is reported in which ulcers of the leg were treated by the application of pinch grafts and in which penicillin was used before and after the grafting to control the surface infection caused by beta hemolytic streptococci and hemolytic *Staphylococcus aureus*. These infections are the chief cause of failure of the skin grafts to take. It is recommended that penicillin be injected intramuscularly before and after grafting of skin in all cases in which ulcer of the leg is treated by pinch grafts.

TREATMENT OF EARLY SYPHILIS WITH PENICILLIN ARTHUR G SCHOCH and LEE J ALEXANDER, J A M A **130** 696 (March 16) 1946

Penicillin properly administered will cure the majority of patients with primary and secondary syphilis. The use of 2,400,000 units of penicillin in seven and a half days (40,000 units intramuscularly every three hours) is advocated. In addition, five intramuscular injections of 0.2 Gm of bismuth salicylate are given at two day intervals. Intimate contacts of the patients should be treated coincidentally to avoid reinfection.

HENSCHEL, Denver

TESTOSTERONE PROPIONATE IN TREATMENT OF SENILE PRURITUS W L DOBES, JACK JONES and ANDREW G FRANKS, J Clin Endocrinol **5** 412 (Dec) 1945

Dobes, Jones and Franks briefly review the literature on the effects of androgens used in the treatment of various dermatoses. After discussing the difficulties in making an accurate diagnosis of "senile" pruritus, they report the results of treat-

ment with testosterone propionate and methyl testosterone—the former administered topically and by injection and the latter given orally. The oral use of methyl testosterone was found to be completely ineffectual. Testosterone propionate by injection was fairly successful in controlling the pruritus but yielded the best result when given subcutaneously.

Both symptoms and visible changes were relieved in 7 patients, and diminished in 2, in 1 there was no relief.

LYNCH, St Paul

SPECIFICITY OF STREPTOCOCCI ISOLATED FROM PATIENTS WITH SKIN DISEASES  
STUDIES ON PEMPHIGUS, DERMATITIS HERPETIFORMIS, LUPUS ERYTHEMATOSUS  
AND ERYTHEMA MULTIFORME ASHTON L WELSH, *J Invest Dermat* 7 7  
(Feb) 1946

The morphologic, cultural, staining and fermentation characteristics of streptococci which were isolated from patients who had pemphigus are described. The streptococci were shown to have a characteristic cataphoretic mobility distribution curve and were found to be virulent for five species of animals. They also produced lesions consistent with those of pemphigus in a few instances.

The different strains of organisms were shown to be serologically identical by (1) agglutination reactions between the various strains and serums of a horse and rabbits which had been immunized against organisms isolated from the patients, (2) reciprocal agglutinin absorption, (3) precipitin reactions between the aforementioned immune serums and alkaline saline extracts of the streptococci isolated from the patients, (4) precipitin reactions between the immune serums and the specific soluble polysaccharide substances, (5) the cataphoretic mobility-reducing action of immune serums, and (6) the reciprocal absorption of the immune serums so that these no longer showed the specific mobility-reducing action.

A specific relationship between the patients who had pemphigus and the streptococci was demonstrated by (1) precipitin reactions between the nasopharyngeal washings and the serums of animals immunized with the specific organisms, (2) precipitin reactions between the blister fluid and the serums of the immunized animals, (3) precipitin reactions between alkaline saline extracts of the organisms and the serums of patients who had pemphigus, (4) precipitin reactions between the specific soluble polysaccharide substances and the serums of these patients, (5) the cataphoretic mobility-reducing action of the patients' serums on the organism, (6) absorption of the antibodies of their serums by heterologous strains of the streptococci so that these serums no longer showed this specific mobility-reducing action, (7) production of bullae in the patients by intradermal and subcutaneous injection of dead organisms and (8) production of the erythema-edema (EE) reaction of Foshay by intradermal injection of immune horse serum.

It was also shown that streptococci isolated from patients who had dermatitis herpetiformis, disseminated lupus erythematosus and erythema multiforme exudativum, respectively, were similar to, but not identical with, the streptococci isolated from patients who had pemphigus.

A NEW TREATMENT FOR ANTHROPOPHILIC TINEA TONSURANS (MICROSPORON  
AUDOUINI) GEORGE MILLER MACKEE, FRANZ HERMANN and FLORENTINE  
L KARP, *J Invest Dermat* 7 43 (Feb) 1946

Based on the results of histologic, mycologic and biochemical experiments, studies were made on the therapeutic effect of trimethyl cetyl ammonium pentachlorophenate in a proprietary vehicle. This fungicide solution was used in combination with an acid-buffered detergent. The treatment resulted in a cure in 54 per cent of the treated patients in approximately fourteen weeks.

This new form of therapy presents a major handicap in the technic of application, and therefore the authors suggest that its use is particularly indicated in those cases in which roentgen ray epilation is not possible or has failed.

EVALUATION OF MEASURES FOR USE AGAINST COMMON FUNGUS INFECTIONS OF SKIN M B SULZBERGER, C SHAW and A KANOF, U S Nav M Bull 45 237 (Aug) 1945

The object of this study was to test the comparative values, for the prophylaxis and the treatment of fungous infections of the feet and the groins, of the following materials (1) undecylenic acid-zinc undecylenate powder, (2) sodium propionate powder, (3) boric acid-salicylic acid powder, (4) undecylenic acid-zinc undecylenate ointment and (5) clothing impregnated with Impregnite CC3 by the water-in-oil emulsion process

The results in prophylaxis revealed that active fungous infections developed in the feet of (1) 885 per cent of the men using no prophylactic measures, (2) 833 per cent of the men who wore an impregnated sock, (3) 1115 per cent of the men using boric acid-salicylic acid powder, (4) 310 per cent of the men using sodium propionate powder, and (5) 107 per cent of the men using undecylenic acid-undecylenate powder

The results in the treatment of active and usually bilateral fungous infections of the feet indicated that (1) Impregnated socks were of no value, (2) propionate powder and undecylenate powder were equally effective, and (3) undecylenic acid-undecylenate powder and undecylenic acid-undecylenate ointment were also equally effective

In the treatment of active fungous infections of the groin, the results were as follows (1) Undecylenic acid-undecylenate powder effected cures in 35 cases and improvement in 8 and was of no effect in 1, (2) sodium propionate powder effected cures in 10 cases and improvement in 3 and was of no effect in 4, and (3) impregnated clothing made the infections in 4 cases worse and was of no effect in 7

ROBIN, South Bend, Ind

ARSENICAL ENCEPHALOPATHY G A RANSOME, J C S PATERSON and L M GUPTA, Brit M J 1 659 (May 12) 1945

Five patients with arsenical encephalopathy were successfully treated by a program which emphasizes the value of the sitting posture for these patients

"Decongestion" can be achieved simply by the patient's sitting up against a back rest Lumbar puncture and dehydration of the brain with concentrated serum albumin or hypertonic dextrose solution were also employed

PENICILLIN CREAM OF LOW CONCENTRATION G H DU BOULAY, Brit M J 1 50 (Jan 12) 1946

Thirty-nine patients with staphylococcic and streptococcic infections of the skin were treated with a penicillin cream containing 200 units of penicillin per cubic centimeter The cream also contained 2 cc of 2-phenoxy-ethanol

The author concludes that if impetigo has been present for five weeks or less it will heal in from three days to two weeks provided treatment is continued until no mark remains on the skin Chronic impetigo and sycosis barbae fail to clear with this cream No evidence of a sensitive strain becoming resistant during treatment was found

DERMATITIS DUE TO SULPHAGUANIDINE BASIL HAIGH, Brit M J 1 52 (Jan 12) 1946

A patient with a probable solar dermatitis, who had an ulcer of the leg, was treated with sulfanilamide powder locally, without success Six weeks later he was given sulfathiazole by mouth, following which a papular eruption developed on the legs and the trunk Two months later he was admitted to the hospital with bacillary dysentery, for which he was given sulfaguanidine Two days later he presented an eruption identical with that of the previous sulfathiazole dermatitis, which was limited to the sunburned areas of the skin The results of patch tests with sulfanilamide and sulfaguanidine on nonsunburned areas were negative

SHAW, Chattanooga, Tenn

# Society Transactions

## MINNESOTA DERMATOLOGICAL SOCIETY

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*Feb 9, 1945*

### **Chronic Lupus Erythematosus of the Face and the Tongue** Presented by DR S E SWEITZER, Minneapolis

E R, a white woman aged 52, first began to have a cutaneous disease in the summer of 1943. The first attack affected both elbows and then the arms and the legs. The entire face and the ears were involved with a red, swollen eruption which included blisters. In the fall of 1943 the eruption subsided, only to recur in the summer of 1944. This second attack involved the same areas as the first, but in the fall it persisted in patches over the nose, the malar region and the lips, behind the ears and on the forearms and the lower portions of the legs. Her health was good until 1933, at which time she contracted amebic dysentery in Chicago. A hysterectomy for fibroids was done that year.

The leukocyte count was 6,600, the differential and the erythrocyte count were normal, as was the urine. The serologic tests for syphilis gave negative results. The tuberculin reaction was strongly positive.

An examination revealed dull red patches, several centimeters in diameter, across the bridge of the nose and on both cheeks. There was also a patch on the dorsum of the left hand and behind the left ear. The plaques were dry and had small adherent scales. On the left side of the tongue near the posterolateral margin was an ill defined irregular plaque.

Histologic sections of the tongue and the cutaneous lesions were shown.

#### DISCUSSION

DR J F MADDEN, St Paul. I think that it is common to have transitory benign plaques like these associated with scrotal tongue. I do not think that the lesions on the tongue are those of lupus erythematosus.

DR L H WINER, Minneapolis. Microscopically, there are follicular dilatation, plugging of the follicles by nucleated cells instead of non-nucleated cells and lymphocytic infiltration. Also favoring the diagnosis of lupus erythematosus is the atrophy of the mucous membrane. One does not see atrophy in transitory benign plaques of the tongue.

DR S E SWEITZER, Minneapolis. I still think that it is a benign transitory plaque.

### **Pemphigus Vulgaris of the Mucous Membrane** Presented by DR H E MICHELSON, Minneapolis

Mrs H M, a white woman aged 56, was first seen at the University Hospitals, Minneapolis, in September 1944, with an eruption in the mouth of about ten years' duration, especially severe for the past three years. No definite bullae were observed on any other part of the body except the mucous membrane of the mouth. Previous medicament consisted of germanin, acetarsone, oxophenarsine hydrochloride, tryparsamide, Asiatic pills (a preparation of arsenic trioxide and black pepper) and sulfapyridine. The patient had a severe reaction from germanin and no improvement from any of the medicaments. Treatment at the University Hos-

pitals consisted of a series of vaccinations with smallpox vaccine. The patient reacted strongly to the first vaccination and remained immune thereafter. No improvement was noted in the lesions of the mucous membrane.

Serologic tests for syphilis were negative. On December 18, 5 mice were inoculated intracerebrally with fluid from the blisters of the roof of the mouth. The animals were observed for five weeks and showed no signs of illness.

An examination showed bullae on the hard palate, the buccal mucosa and the inner surfaces of the lips. Erosions of the sites of ruptured bullae are present.

#### DISCUSSION

There was no discussion of this case.

#### Lichen Planus of the Mucous Membrane and the Eyelid Presented by DR L. H. WINER, Minneapolis

Mrs. A. A., a white woman aged 40, stated that an eruption broke out in her mouth in July 1944. About a month later a lesion formed on the right lower eyelid. She had been treated by a physician and a dentist for Vincent's infection of the mouth. In the past two weeks the gums had become eroded and tender at the border of the teeth. In the past eight weeks she received 1 cc. of 10 per cent bismuth subsalicylate in oil once a week intramuscularly.

On examination the buccal mucosa of each cheek showed whitish papules, arranged in rings and striations. The right lower eyelid had a plaque measuring 1 by 1 cm. The border of this red plaque consisted of discrete angulated small papules.

The histologic examination of a biopsy specimen from a papule of the right wrist showed the epidermis hyperkeratotic and the epidermal cells undergoing eosinophilic degeneration. There was the typical vesicular degeneration of the basal cells and formation of Joseph's spaces in the epidermis-cutis border. There was a dense round cell infiltration in the upper part of the cutis which closely approximated the epidermis and had a sharp lower border. This lower border extended to the reticular layer of the cutis, which itself was otherwise uninvolved.

#### DISCUSSION

There was no discussion of this case.

#### Nevus Unius Lateris Presented by DR S. E. SWEITZER, Minneapolis

W. D., an Indian woman aged 20, was admitted to the Minneapolis General Hospital for delivery of her first child on Jan. 30, 1945. She stated that a birthmark had always been present on her left cheek and over her left ear but that during the past year it almost doubled its size.

An examination revealed a brownish gray irregular tumor, the size, the shape and the thickness of a man's thumb, extending down over the left cheek. The tumor became smaller as it curved over the left ear and gradually disappeared behind the ear. The mass was somewhat tender, and pressure expressed a thick whitish material from crevices which gave a lobulated appearance to the tumor. The rest of the skin was normal save for a coffee-colored spot, measuring 3 by 2 cm., on the internal surface of the left arm.

Histologic sections were shown.

#### DISCUSSION

There was no discussion of this case.

#### Lingua Nigra Presented by DR S. E. SWEITZER, Minneapolis

M. K., a white woman aged 27, stated that her tongue first became black eight months ago and that it remained so for two months. There have been several recurrences since, lasting for a few days. Three weeks ago it again became



black. She stated that on the basis of a papular eruption a diagnosis of syphilis was made in September 1944 and she was given eleven intramuscular injections. In November she entered the Minneapolis Treatment Center and was given 1,200,000 units of penicillin over a period of eight days.

An examination revealed a brownish black coating covering the posterior two thirds of the tongue on its dorsal surface. The papillae are slightly hypertrophic, but no long, hairlike lesions were seen.

#### DISCUSSION

There was no discussion of this case.

#### Abortive von Recklinghausen's Disease Presented by DR S E SWEITZER, Minneapolis

C P, a white woman aged 66, has had lesions on her right forearm since she was 21 years of age. Small nodules developed on the right forearm, increased to their present size rather quickly and have remained stationary ever since. The patient's general health had always been good except that in 1930 the uterus was removed because of fibroids. There was no history of any cutaneous tumors in any members of her family. Roentgenograms showed that the long bones were normal.

An examination revealed twenty to thirty small nodules, varying in size from that of a pinhead to that of a pea. The only area involved is the anterior surface of the right forearm. The nodules are flesh colored and soft and are not painful. There are several scars due to the removal of the lesions by cautery. The rest of the body is clear. There is no hyperpigmentation.

Microscopic sections were shown.

#### DISCUSSION

DR L H WINER, Minneapolis: About six weeks ago I had occasion to use radon ointment on ulcers of the leg and had some left over. On that day a patient with granuloma annulare came in, and I put some of the radon ointment (200 electrostatic skin units per cubic centimeter) on three of the lesions. The following week I put radon ointment (200 electrostatic skin units per cubic centimeter) on again for twenty-four hours. I saw the patient yesterday, and the lesions have disappeared, leaving only brown spots.

DR S E SWEITZER, Minneapolis: What is in the solution?

DR L H WINER, Minneapolis: Radium emanation in petrolatum. It loses 7 per cent of its strength each day.

DR S E SWEITZER, Minneapolis: The emanation is gone in practically four days.

#### A Case for Diagnosis (Pityriasis Rubra Pilaris in One of Twin Brothers?).

Presented by DR L H WINER, Minneapolis

S I, a boy aged 14, complains of painful fissures and thickening of the skin of the palms and the soles for the past year. This condition was aggravated during the cold weather of the winter months and improved during the summer. He also gave a history of having had hay fever, for which he has been treated.

The skin on his palms is thickened and fissured, as is the skin on his soles. The dorsal aspect of the fingers shows thickening and redness of the skin over the knuckles. There is also a plaque of dermatitis on his left elbow. Granular lesions about 1 mm in diameter can be seen on the mucous membrane of the anterior tonsillar fold just above the level of the lower molar teeth.

#### DISCUSSION

DR PAUL O'LEARY, Rochester, Minn.: The lesions have the earmarks of a neurodermatitis rather than those of pityriasis rubra pilaris. The plaque on the left elbow of comparatively recent origin is of the type of lichen chronicus simplex.

DR L H WINER, Minneapolis Dr Sweitzer also saw this patient, and he thought that there probably was a vitamin A deficiency He has been given 100,000 units of vitamin A for a period of two months However, I feel the same as Dr Sweitzer, that this is a keratosis on the basis of a vitamin A deficiency

**Pityriasis Lichenoides et Varioliformis Acuta** Presented by DR S E SWEITZER, Minneapolis

D B, a boy aged 6 years, first noticed small red lesions on the right forearm near the shoulder one year ago A few more lesions developed, and then the patient contracted measles Following this, additional scaling, crusting and papular lesions developed over the entire body These lesions have disappeared and reappeared since that time, and many have healed, leaving 'a fine atrophic scar There was no itching or other symptom, and his general health was always good

An examination revealed scattered erythematous papules with scaling and crusting over the face, the trunk and the extremities They are 3 to 5 mm in diameter, some show a thick crust, and others show a thin silvered scale Many scars point out the location of previous lesions

The histologic examination of a recent (young) lesion showed a parakeratotic scale which lay on a fairly normal epidermis The basal cells of the epidermis in this involved area were difficult to differentiate from the cells of the cutis in that the epidermis took a more intense eosinophilic stain There were faint suggestions of vesicle formation in the epidermis underneath the parakeratotic scales The cutis contained a moderately heavy perivascular round cell infiltration The connective tissue stained deeply with eosin, and the lymphatic spaces were intensely dilated

**Rosacea of the Nose Tuberculoid Structure in Histologic Section** Presented by DR L H WINER, Minneapolis

Mrs G C, a white woman aged 62, has had an eruption on the nose for the past ten years Three years ago, after roentgen ray treatment, it disappeared, but during the present winter it has recurred

On examination the skin on the tip of the nose was thick and boggy and showed numerous small nodules, 1 to 2 mm in size, which were red and were completely expressed on diascopy A test with old tuberculin (1:1,000) elicited a negative reaction Treatment consisted of applications of peeling pastes, which produced an improvement

Histologic sections were shown

DISCUSSION

DR S E SWEITZER, Minneapolis I thought that this case ought to be presented because some cases have been presented as rosacea-like tuberculoid of Lewandowski and many are not really cases of tuberculosis

DR FRANCIS LYNCH, St Paul Are the microscopic changes truly tuberculoid or only those of chronic granulomatous inflammation? It is not a typical tuberculoid structure

DR L H WINER, Minneapolis I do not know of any other way of putting the point across

DR FRANCIS LYNCH, St Paul It is not a typical tuberculoid structure

DR L H WINER, Minneapolis Tuberculoid, yes, but not tuberculous

**Pyoderma Faciale**, Presented by DR S E SWEITZER, Minneapolis

A H, a white woman aged 23, first had an eruption on the face in 1938 during her first pregnancy This eruption subsided two months after delivery In 1941 it recurred at the sixth month of the second pregnancy, and she was seen in the

outpatient department of the Minneapolis General Hospital, at which time a diagnosis of rosacea was made. This attack lasted for two years, after which her skin was completely clear. There were no deep pustular elements or tendency toward scar formation at that time. The third recurrence began in October of 1943, at the beginning of the third pregnancy, and became progressively worse. After delivery a large amount of pus drained from the sinuses, and boggy hypertrophic nodules appeared. She was seen in the outpatient department of Minneapolis General Hospital in September of 1944, at which time pustular and keloidal elements involved the forehead, the face and the submental area. The rest of the body remained completely free. There was no previous history of cutaneous disease. The general health has always been good. Serologic tests for syphilis were negative. The results of hematologic and urinary studies were within normal limits. In treatment 1,500,000 units of penicillin was administered between September 30 and November 8. After the administration of penicillin the pustular discharge improved greatly, and between Nov 21, 1944, and this date she has received eight roentgen ray treatments (88 r each) at weekly intervals.

An examination revealed bluish red nodules and linear hypertrophic scars on the forehead, the face and the submental areas. There is no suppuration at the present time.

#### DISCUSSION

DR PAUL O'LEARY, Rochester, Minn. This woman looked considerably older than 23. The history I obtained is identical with that of many of the girls who have pyoderma faciale. Since her last pregnancy she has gained 40 or more pounds (18 or more kilograms) and has had amenorrhea. The pyoderma, obesity and amenorrhea appeared simultaneously. I have been repeatedly impressed with the frequency of menstrual dysfunction and this eruption, so much so that my therapeutic efforts are directed mainly toward reestablishing a normal menstrual cycle. Cultures from the burrowing tracts are usually sterile, hence antiseptics taken locally or by mouth are directed only to the secondary infection that occurs in these lesions after they are manipulated. The gynecologists should determine the type of ovarian dysfunction she has and direct their efforts to correcting it.

The significance of the part glandular dysfunction plays in this disease is noted especially in the unmarried young women with pyoderma faciale who are underweight, flat chested, anemic and amenorrheic. Not only does the eruption abate with the proper glandular therapy, but also there is a striking improvement in the patient as noted by gain in weight, enlargement of the breasts, return of menses and other physical changes. All the dysfunctions noted in these young women are not of the same type, hence it is not possible to give them all the same glandular therapy. Consequently each case must be evaluated individually.

Roentgen ray therapy has also helped some of my patients, especially those in whom the ovarian dysfunction was not clearcut.

DR C D FREEMAN, St Paul. I gave the patient penicillin, without any results. With sulfathiazole I got excellent results.

DR PAUL O'LEARY, Rochester, Minn. It has been my experience in culturing material from the sinus tract that the cultures have been essentially sterile.

DR J F MADDEN, St Paul. I have been giving sulfathiazole by mouth combined with the usual treatment for acne associated with large abscesses and have obtained much better results than I ever have with any other treatment.

#### Bullous Lichen Planus Presented by DR S E SWEITZER, Minneapolis

M DeF, a white woman aged 29, was presented on Sept 15, 1944 at the meeting of the Minnesota Dermatological Society as having bullous lichen planus. At that time large bullae were present on the arms and the legs, with a few lesions on the abdomen. Typical papules of lichen planus were also present. Shortly afterward the eruption became generalized and involved the entire body, including the face. The patient was hospitalized, and wet compresses were used. Sodium salicylate and sulfadiazine were each tried with no effect, and on Oct 12,

1944 treatment with acetarsone was begun according to the Oppenheim technic. There was decided improvement during the first week, and the treatment was continued until Jan 15, 1945.

An examination as of this date showed only pigmented scars, mostly on the lower extremities but with a few on the arms, the abdomen and the back.

#### DISCUSSION

There was no discussion of this case.

#### Atrophoderma Hypoestrogenicum Presented by DR S E SWEITZER and DR L H WINER, Minneapolis

M T, a white woman aged 30, has had a plaque type of eruption since she was 11 years old. It first began as a small reddish area on the anterior surface of her ankle and spread to involve both extremities. In the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (24 842 [Nov] 1931) she was presented by one of us (S E S) as having *tuberculide en plaque*. At puberty there was about one year of freedom from the eruption, but it recurred in the form of 1 to 5 cm oval or round or gyrate plaques elevated above the surface of the skin. There was a tendency for the lesions to group, and they were never scaly. The color was dusky red, and the atrophic scars of previous lesions were visible. The extremities were the only sites of the eruption. She had borne two children, one in 1939 and the second in 1943. During the fourth month of each pregnancy, the eruption completely cleared only to reappear the fourth or the fifth month post partum. A diagnosis of latent syphilis was made in 1934 on the basis of positive serologic tests. Between 1934 and 1937 she received routine antisyphilitic treatment. Tuberculin reactions have always been negative. Serologic tests for syphilis have been negative since 1936. Leukocytes numbered 7,000 on Dec 1, 1944, and 10,150 on December 23. The differential count showed 5 per cent lymphocytes on December 23. The blood cholesterol level was 150 mg per hundred cubic centimeters in October 1944. On several occasions roentgenograms showed that the chest and the long bones were normal. On October 12 diethylstilbestrol was given, and the dose was increased so that after one week she was taking 15 mg daily. This was continued until November 2 when it was discontinued until December 5. Since then she has been taking 3 mg daily for two weeks out of every month, with little effect on normal menstruation. Two months after diethylstilbestrol therapy was started there was a spectacular abatement in the eruption, the lesions having faded and flattened.

An examination revealed a few lightly pigmented areas, 2 or 3 cm in diameter, on the upper extremities, which were the remains of previous plaques. A few slightly raised purplish plaques, 2 to 4 cm in diameter, remained on the lower extremity at the site of the previous eruption.

Histologic sections were shown.

#### DISCUSSION

DR S E SWEITZER, Minneapolis. Dr Winer has been taking care of the patient for years. Her eruption comes and goes.

DR STEPHEN ROTHMAN, Chicago. I should like to ask whether or not the patient has hyperthyroidism. She displays a slight degree of exophthalmos.

DR L H WINER, Minneapolis. Her basal metabolic rate was normal. Also her blood cholesterol level was 150 mg per hundred cubic centimeters.

DR H E MICHELSON, Minneapolis. How do you correlate all the findings in this patient 19 years of age? Why the giant cells? Is there any relationship between the theelin and the findings?

DR L H WINER, Minneapolis. In view of the history of these lesions occurring and disappearing with pregnancy and recurring after pregnancy, this patient was shown to Dr John McKelvey. He advised giving her diethylstilbestrol, 5 mg, three times a day. Two biopsies were made of two of the active lesions.

From a microscopic section and on staining a frozen section for fats, it was found that there was an excessive amount of fat in the infiltrated zone. The pathologist could give no help on any differential stains to show specificity of the fat. The reason I mention fat is that the fat could account for the formation of giant cells, because capsule lipids of the tubercle bacillus have been known to cause formation of giant cells. After the inflammation receded, the microscopic section showed a reduced cellular infiltration and also a reduction in the amount of fat in the tissue. The elastic tissue in these areas was gone. Because the elastic tissue has disappeared and the skin shows atrophy clinically, we decided to call it atrophy. We call it hypoerogenic because the resorption occurred with the administration of stilbestrol. We are still doubtful of this patient's maintenance dose of stilbestrol. We stopped giving her stilbestrol two weeks ago, after she had taken 1 mg three times a day for two weeks. She started to menstruate six days ago and is still menstruating. It is unusual for her to menstruate so much. Dr John McKelvey suggested that we reduce the dose of stilbestrol to 3 mg per day because he thought that we might get hypertrophy of the endometrium which might necessitate the removal of the uterus. With that idea in mind, we have made platelet counts, which were within normal limits, 300,000 per cubic millimeter.

DR CARL LAYMON, Minneapolis. In my opinion the term "atrophyderma hypoerogenicum" does not fit this case. There is no atrophy, and except for the history of improvement during pregnancy there is nothing which even pertains to ovarian function. The patient has no signs of a lack of estrogens and has had two normal pregnancies. The lesions clinically fit better a diagnosis of sarcoid, and even the histologic data can be fitted in with such a diagnosis.

DR S E SWEITZER, Minneapolis. I suggest that if she is having trouble menstruating she had better stop the stilbestrol. It only seems to alleviate the condition.

DR FRANCIS LYNCH, St Paul. The disappearance of her eruption at puberty throws considerable doubt on the thought that the eruption results from estrogenic deficiency. Perhaps some other endocrine disturbance is responsible.

DR S E SWEITZER, Minneapolis. I think that either sarcoid or tuberculosis is the proper diagnosis in this case. I was never much inclined to this hypoerogenic diagnosis in her case, but Dr Winer wanted to see what he could do with the eruption, so I let him.

#### **Dermatitis Medicamentosa** Presented by DR S E SWEITZER, Minneapolis

L H., a white woman aged 34, was taking phenobarbital,  $\frac{1}{2}$  grain (30 mg) three times a day, because of high blood pressure. She also was taking a capsule containing sodium iodide, phenobarbital and theobromine. The use of both these drugs was begun two weeks before the onset of the eruption. An ovarian cyst was removed in March 1944, and a gynecologic operation was performed in 1930. Three weeks ago she was seen in the Minneapolis General Hospital with a general scarlatiniform eruption. It also involved the conjunctivas, the lips, the entire mouth and the throat, which were intensely red and dry, the mucous membrane resembled that of previous patients with eruption due to phenobarbital. On the legs and the lower part of the abdomen the eruptions were morbilliform. The temperature of the patient on admission to the hospital was 105 F. The leukocyte count was 3,800, of which 92 per cent were lymphocytes. There was a gradual fading of the color of the eruption.

An examination revealed a dull red skin, especially pronounced on the face. There was slight scaling of the face and the backs of the hands. The mucous membranes were still dry and injected.

#### **DISCUSSION**

DR S E SWEITZER, Minneapolis. I recall the deaths of 3 patients who had dry red skins, dry red mouths and tongues and high temperatures. This girl took extremely small doses of phenobarbital and had a high temperature.

**Keratosi Blennorrhagica** Presented by DR S E SWEITZER, Minneapolis

R D, a white man aged 23, first noticed a urethral discharge five weeks ago. For three weeks he did nothing about it, and on Jan 23, 1945 he was admitted to the Minneapolis General Hospital with acute gonorrheal urethritis and acute arthritis involving the left ankle, knee and wrist and the little finger of the left hand. His temperature ranged between 100 and 102 F, and he had a leukocyte count of 13,400. Urethral smears have been positive for gonococci. On January 23 he began to take sulfadiazine, 1 Gm every four hours, and on January 25, because his condition was becoming worse, he was given 300,000 units of penicillin over the next four days. The lesions on the feet have been present for two weeks.

An examination revealed diffuse thickening on the plantar surfaces of both feet. Irregularly arranged over this area were hornlike projections from split pea to hazelnut size. On the dorsum of the left hand and wrist and on the left knee and ankle are numerous large vesicles and crusts. These areas have been subjected to hot packs.

## DISCUSSION

DR PAUL O'LEARY, Rochester, Minn. Some of the members are no doubt familiar with the syndrome recently described by Dr Reiter, in which there is a urethral discharge in which gonococci are not demonstrable, associated with conjunctivitis, arthritis and a bizarre type of dermatitis. Several of my former associates have seen soldiers who returned from overseas with the syndrome. The small amount of penicillin which was given this patient at long intervals might account for the lack of improvement, and it would seem advisable to try it again, with at least 1,000,000 units being given in a period of three days. The smears from the urethral discharge were positive for gonococci, but as I understand the matter they became negative before the penicillin was given.

Keratosi blennorrhagica is an extremely rare disease in my experience, and accordingly the clinical picture is far from clear in my mind. Patients with chronic infectious arthritis of nongonorrheal origin will occasionally display inspissated and hyperkeratotic lesions, especially if the nursing care has been neglected. The study of Reiter's syndrome and gonorrheal keratosi blennorrhagica should be combined with the hope of eliciting some additional information about both diseases.

DR STEPHEN ROTHMAN, Chicago. I saw 2 cases of keratosi blennorrhagica. In both cases gonococcic septicemia was present, and both patients had arthritis and endocarditis. In the beginning both neglected their gonorrhea, and each went to see a physician after he had had severe prostatitis for several weeks. Diffuse keratoses, but no papular elements as in the presented case, were present on the soles, the palms and the elbows. Both patients died, because this happened long before the era of modern chemotherapy. I should like to ask whether penicillin has been used in gonococcic endocarditis and septicemia and with what result.

DR PAUL O'LEARY, Rochester, Minn. I have had no experience, although reports are indicated.

DR STEPHEN ROTHMAN, Chicago. I hear that in the presented case the keratosi did not respond to penicillin.

DR PAUL O'LEARY, Rochester, Minn. It might be the small dose and that there was a lapse of time. It might be that a million units would make a different picture.

**Squamous Cell Epithelioma of Sebaceous Gland Origin** Presented by DR S E SWEITZER, Minneapolis

M H, a white man aged 77, has had a tumor on the back of his neck for three years. At times it broke open and ulcerated. Twenty-five years ago a cancer was removed from the right cheek with radium. In 1937 roentgen rays were successfully applied to an epithelioma on the right side of the nose, and in 1939 cautery was used on a lesion of the right temple.

An examination revealed the scars of the three previous lesions. On the back of the neck was a button-like tumor, 2 cm in diameter. The tumor was red and had a slight central depression. It was entirely above the surface of the skin and freely movable.

The histologic examination showed the epidermis to be present in some areas and absent in others and the tissue to be ulcerated. Lying beneath the epidermis and in the ulcerated area were nests of cells well walled off, the contour of which assumed that of sebaceous glands, and these cells in the basal zones appeared foamy as do sebaceous cells. In other zones higher up or more toward the center of the proliferating mass, these cells had become keratinized, and the nuclei had become darker and contained mitotic figures.

#### DISCUSSION

DR STEPHAN EPSTEIN, Marshfield, Wis. This is a somewhat odd tumor. Clinically it looks like a basal cell epithelioma, being made of a rather soft grayish translucent tissue. The location at the back of the neck is somewhat unusual.

Microscopically it is an atypical tumor composed mostly of cells with dark-staining nuclei, many of them spindle shaped, presenting the appearance of basal cells. There are a few spots where an attempt at pearl formation is made. However, these are not real horn pearls but what Darier called parakeratotic pearls. This picture would fit in well with that type of epithelioma that is called by Darier *epithelioma metatypique nure*.

DR L. H. WINER, Minneapolis. Dr. Hamilton Montgomery calls these cells "cells with individual cell keratinization." Ordinarily the sebaceous cell is a basal cell which secretes, but when a basal cell forms keratin and shows mitoses, as some of these cells do, then it is called a squamous cell epithelioma.

#### Macular Atrophy Presented by DR S. E. SWEITZER, Minneapolis

L. H., a white woman aged 70, has had generalized itching of the skin for the past six months. She was not aware of the presence of white spots.

An examination disclosed irregular whitish spots with wrinkled, atrophic skin. The lesions were grouped and extended along the upper part of the chest over the clavicle and on to the side of the neck. One or two of the areas showed follicular plugging.

The histologic examination revealed hyperkeratosis and also epidermal atrophy in the sense that the papillary bodies had disappeared. The sebaceous glands were absent, but the sweat glands were present. The upper portion of the cutis showed zones of homogenization, under which there were bands of round cell infiltration.

#### DISCUSSION

DR STEPHEN ROTHMAN, Chicago. This woman is suffering from an inflammatory eruption. She states that she has had generalized itching for the past six months, and now diffuse reddening and scaling can be seen. There are a few atrophic scars in the inflamed areas, but I do not see any sign of idiopathic atrophy. The histologic section does not substantiate this diagnosis either. It is true that macular atrophy, or anetoderma of Jadassohn, is described as starting with mild inflammation, but this is of short duration. It is my feeling that the initial inflammatory phase has been overemphasized in the literature. The essential primary change in macular atrophy is atrophy of the elastic fibers.

DR PAUL O'LEARY, Rochester, Minn. The atrophic plaques on the left side of the neck had definite plugs which suggested the diagnosis of lichen sclerosus et atrophicus.

DR FRANCIS LYNCH, St. Paul. On the chest, especially under the breast, one can see shiny flat papules, of pinhead size, fairly characteristic of lichen sclerosus et atrophicus. The sections do not confirm that diagnosis, but the tissue was removed from a site where a complicating dermatitis is present.

**Keratosis Follicularis** Presented by DR S E SWEITZER, Minneapolis

J S, a white man aged 74, was presented at the meeting of the Minnesota Dermatological Society on April 14, 1939. The eruption has been present as long as he can remember, and in recent years he has had no treatment. The eruption has progressed and is more extensive than it was in 1939. In January of 1945 his left leg was removed because of arteriosclerotic gangrene.

A moist eruption is seen in the groins and axillae and on the sides of the neck. It is covered with a greasy scale, and is foul smelling. Toward the periphery of the moist plaques the eruption becomes distinctly papular with crusted lesions, 3 to 5 mm, which are present also on the lower part of the abdomen and on the back.

The histologic examination of the thinner of the two biopsy specimens revealed hyperkeratosis with extreme formation of lacunae in the epidermis. A few *corps ronds* were seen in the region of the epidermis which formed the floor of the lacunae. Grain cells were not in evidence in this section.

## DISCUSSION

There was no discussion of this case.

**Mycosis Fungoides** Presented by DR S E SWEITZER, Minneapolis

A A, a white woman aged 72, has had an eruption for the past ten years. At no time was the skin completely clear, but there has been one episode after another of exacerbation and remission, with the exacerbations becoming more severe and prolonged in recent years. She was admitted to the Minneapolis General Hospital fifteen times during the past five years. The eruption was confined mainly to the following sites: face, ears, scalp, neck, axillae, submammary regions, umbilicus, groin, popliteal spaces and the lower portions of the legs. There has always been much edema with exudation and fissuring to form ill defined plaques, on which later moderately thick but loosely adherent white scales develop. Greases have been poorly tolerated, and roentgen rays in fractional doses did not help. The involved areas have responded best to wet packs and lotions. Itching has never been a prominent feature, but excoriations have often been present.

From 1940 to 1942 the leukocyte count ranged from 5,000 to 7,000, with a normal differential count, but since 1943 there has been leukopenia (from 1,800 to 4,000 cells) 40 to 60 per cent of the cells being lymphocytes. In June 1944 a biopsy of sternal bone marrow was performed, and numerous reticulocytes were seen which were thought to be of a low grade malignancy. Cutaneous imprints, taken in June and subsequently stained with Wright's stain show the same immature reticulum cells to be present in the skin.

Serologic tests for syphilis were negative. Other laboratory procedures revealed no abnormalities with the exception of occasional albumin in the urine. A tuberculin test elicited a positive reaction. The previous health of the patient was good except for a drainage of the gallbladder in 1924 and a vein-stripping operation for varicosities of the lower extremities years ago. There have been occasional spells of vertigo and weakness, and one month ago the patient had an attack of cystitis.

An examination revealed an ill defined scaly eruption on the face, the ears and the abdomen, beneath the breasts, in the groins and on the lower extremities. In the groins, the axillae and the popliteal spaces and behind the left ear there is a tendency toward fissuring and exudation. The scalp is thickly covered with a gray adherent scale. When the scale is removed from the lesions of the glabrous skin, a bright red base is revealed.

Specimens of bone marrow, imprints of the skin and sections stained with hematoxylin and eosin were shown.

## DISCUSSION

DR STEPHAN EPSTEIN, Marshfield, Wis. Roentgen ray treatment of mycosis fungoides should be individualized. Some patients respond remarkably well to



small doses, whereas others require relatively larger single doses, such as 300 r, even in the pretumor stage. One might hesitate in this case to give further roentgen ray treatments on account of the low white cell count. In such a case, treatment with alpha rays is sometimes helpful. I mention this because ointments giving off alpha rays are now available, such as the radon ointment. Years ago I treated several patients with thorium X ointment, another means of applying alpha rays. The results were gratifying, in some instances, although only temporarily. An ointment containing at least 2,000 electrostatic units is advisable.

DR EMIL SCHLEICHER, Minneapolis (by invitation). This brings up the point I want to mention. The treatment is invariable, relieving no symptoms.

DR STEPHEN ROTHMAN, Chicago. It is remarkable that the patient does not complain of itching and says that she has never scratched the lesions. On clinical grounds I doubt that this is mycosis fungoides.

DR L. H. WINER, Minneapolis. A microscopic section shows an infiltration of reticulum cells which are active—not so active, however, as in Hodgkin's disease of the skin. It was because of this biopsy of the skin that Dr. E. Schleicher, the hematologist, was called in to make studies of bone marrow, and he was able to observe these malignant cells both in the marrow and in imprints of the skin. The severe leukopenia that this patient has is something which was also explained on the basis of the malignant cells. Dr. Schleicher, will you explain the leukopenia?

DR EMIL SCHLEICHER, Minneapolis (by invitation). In my opinion this is not a case of mycosis fungoides but a low grade malignant reticuloendothelioma. The highly malignant type has been seen in Mrs. S., and, as will be remembered, leukopenia was the outstanding associated symptom. The leukopenia may be explained on the basis that the tumor cells or the reticulum cells replace the myeloid tissue or that the tumor is highly toxic to the myeloid tissue. In the latter case leukopenia results from arrest of the maturation of the myeloid tissue. At this point I wish to mention that the term "reticulocyte" has been used in the outline, a term which designates an immature red cell. The term "reticulum cell" is correct. In my experience the therapeutic application of roentgen rays and radium has given only temporary relief. This has been pointed out also by Dr. Epstein. We have seen complete disappearance of the cutaneous lesions as well as of tumors within twenty-four to forty-eight hours, and the symptoms did not recur at any time over periods of from one month to six months. It has been shown by serial biopsies that the tumor is not killed, that a small number of mitotic figures are demonstrable in the histologic preparations. On recurrence the tumor invasion is usually much more severe than it was before therapy. This has led to the belief that radiation, while suppressing the tumor growth, will either stimulate the tumor per se or bring a change in the surrounding tissue. As an example, I wish to cite the case of Mrs. S. Recurrence of the tumors was noted within four weeks after their retrogression. The histologic structure of the low grade malignant reticuloendothelioma or reticuloma is well presented in the histologic preparation shown today under the microscope. The lesion is not difficult to recognize, because of the extensive hyperplasia of the reticulum. Further, one has seen these reticulum cells, with their large elliptic or round nuclei and abundant light-staining cytoplasm, in the cutaneous imprint. Moreover, the bone marrow was demonstrated in the form of a histologic preparation, and, as will have been noted, the hyperplasia of the reticulum is in every respect malignant, at its periphery there is an inflammatory zone consisting of small lymphocytes, eosinophils and macrophages. The lesion in the marrow is exceedingly early. I am unable to state how soon the marrow will be completely replaced by this process.

DR PAUL O'LEARY, Rochester, Minn. I still find chaulmoogra oil and fever therapy of help in treating patients with mycotic fungoides. The use of chaulmoogra oil was suggested by Lomholt, of Copenhagen, and I added the fever therapy to the program because it seemed to me that when used alone fever moderated the itching somewhat. It might be that I have unwittingly given this treatment to patients who have had the milder forms of mycosis fungoides, but

in any event the course of the disease has been slow after the treatment in all my cases. I agree with the patients who suggested that roentgen ray therapy seemed more efficient after the course of treatment with chaulmoogra oil and fever—evidenced by the rapidity with which the plaques melt out under lesser doses of roentgen rays.

DR STEPHEN ROTHMAN, Chicago. I have been much interested in Dr O'Leary's remark. On record is the case of a patient who for the last two years was completely free of signs and symptoms. He had clinically typical premycotic lesions and numerous large tumors. The histologic data also were typical of mycosis fungoides. He obtained as much roentgen ray irradiation as was permissible, but the lesions and tumors did not clear completely. Treatment with ethyl chaulmoograte was continued for several months. In the management of mycosis fungoides with roentgen rays alone, I never experienced such long periods without relapse. I should like to ask Dr O'Leary what dosage he uses.

DR PAUL O'LEARY, Rochester, Minn. The chaulmoogra oil is given intramuscularly in doses of from 2 to 6 cc every day for approximately thirty injections while the patient is receiving five to eight hyperthermy treatments. I have given as much as 15 cc of Chaulmestrol per day. I want to avoid giving the impression that mycosis fungoides is cured by chaulmoogra oil and hyperthermy, but I am convinced that it makes the disease less of a burden to the patient.

**Synovial Lesion of the Finger** Presented by DR L. H. WINER, Minneapolis

Mrs. P. J. F., a white woman aged 57, two years ago had a similar lesion at the site of the present one. It disappeared spontaneously but recurred in the past six months and gradually enlarged.

On the dorsum of the terminal phalanx of the left middle finger, just distal to the terminal interphalangeal joint and to one side of the midline, is a globular cystic mass measuring 12 by 7 mm. It is 3 mm in height. It is painless to pressure and white.

The patient also has arthritis of the fingers of the right hand, which are stiff. The lesion is being treated with roentgen rays.

#### DISCUSSION

DR L. H. WINER, Minneapolis. I showed this patient because she also is being treated by a colleague for arthritis. This physician said that he sees 10 to 15 such patients a week and that the lesion is simply an enlargement of the capsule of the joint with gelatinous contents. He expresses the contents after piercing the capsule with a needle, and the joint gets well in a few days. My experiences have been quite the contrary. I have been treating such joints with roentgen rays, and they are slow in responding. Others have been excising the involved tissues with ulcers and draining sinuses resulting.

**Chancroid?** Presented by DR S. E. SWEITZER, Minneapolis

C. S., a white man aged 44, was admitted to the Minneapolis General Hospital on February 8. Four weeks ago, five days after exposure, he noticed a lesion on the dorsum of his penis. The sore was not painful and caused him no discomfort. The lesion gradually enlarged. Serologic tests for syphilis were weakly positive. A smear did not show the presence of Ducrey's bacillus. Cutaneous testing with an antigen prepared from a culture of Ducrey's bacillus and auto-inoculation have been done. Dark field examination failed to show the presence of *Treponema pallidum*.

An examination revealed a large oval ulcer, 2.5 to 3 cm in diameter, on the dorsum of the penis. There is crusting as well as a pustular discharge. There is moderate enlargement of the inguinal lymph nodes, which are painless and discrete.

## DISCUSSION

DR PAUL O'LEARY, Rochester, Minn About 1 case of chancroid a year is seen at the Mayo clinic Last year Dr Day and I saw a young married woman with chancroids of four days' duration Her husband, a sailor, had a chancroid in January 1944, which was treated with a sulfonamide compound, and a rapid disappearance of the lesion followed He returned home in September 1944, and five days after he arrived home his wife had lesions which were subsequently diagnosed as chancroids She was intolerant of the sulfonamide compounds, hence penicillin was given, with a complete disappearance of the lesions An examination of her husband did not reveal a lesion of any type on his genitalia, cultures of material from the prostate, stimulating irrigations of the urethra and manipulation failed to obtain a positive culture for *Haemophilus ducreyi* I feel certain that the wife had no extramarital exposure Women without demonstrable ulcerations have been found to be carriers of *H ducreyi*, but it is rarely that a man has been thought to be a carrier when he has no obvious lesions of the genitalia

**A Case for Diagnosis (Sporotrichosis?)** Presented by DR J F MADDEN, St Paul

D R, a school boy aged 12, skinned a rabbit on Nov 1, 1944 About a week later an abscess appeared on the dorsum of the right index finger, over the first phalangeal joint This was incised by his local physician At intervals of a few days several nodules and abscesses began to appear and extend up the arm Some of these ulcerated, and others remained as hard painless marble-sized red nodules At present there are two irregular olive-sized fungating lesions on the dorsum of the hand and several nodules varying in size from that of a marble to that of an olive, on the forearm and the arm, extending from the fingers to the shoulder The lesions are asymptomatic There is also an olive-sized ulcer on the lateral surface of the middle third of the left leg There was no history of previous injury to the hand The patient feels well, and his temperature is normal Three agglutination tests for tularemia were negative, the last one being made the first week of January 1945 The Wassermann test of the blood was negative The Mantoux test with a 1:1,000 solution of old tuberculin elicited a negative reaction A biopsy specimen was shown Fungi were not found in fresh preparations made with sodium hydroxide

## DISCUSSION

DR STEPHEN ROTHMAN, Chicago This morning Dr Madden showed me the culture tubes, but it was impossible to identify the colonies, because of heavy bacterial contamination Clinically, I think, the best diagnosis is sporotrichosis

DR FRANCIS LUNCH, St Paul Have iodides been given?

DR J F MADDEN, St Paul No

DR C D FREEMAN, St Paul I do not believe that one may contract tularemia in Minnesota during the month of February since all the rabbits infected with tularemia are long since dead I am definitely satisfied that this is a case of sporotrichosis

DR H E MICHELSON, Minneapolis Sporotrichosis can be found in plants Why is it so rare in human beings?

DR STEPHEN ROTHMAN, Chicago Apparently sporotrichosis is not widespread in this country It is rather common in Europe Many cases have been reported in which the infection could be related to an injury incurred by walking barefooted in fields and among bushes or by pricking the skin of the finger on thorns of plants The formation of real abscesses is rather characteristic

DR J F MADDEN, St Paul Most of the lesions were abscesses, which were incised by his family physician

## LOS ANGELES DERMATOLOGICAL SOCIETY

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Feb 13, 1945

**Granuloma Annulare Disseminated Type** Presented by DR SAMUEL AYRES JR

N T, a white girl aged 8 years, had an acute attack of urticaria at the age of 2 years. The present eruption, beginning seven months ago, was the next disease of the skin. The first lesions appeared on the buttocks. Mild itching was present at the onset, but now there is no itching. Lesions have appeared on the thighs and the trunk in the past two months.

The lesions are widely scattered, but they are most abundant over the medial portions of the buttocks. They are rather indistinct, pale pink areas. Some are as small as 6 mm in diameter, and others are 2 cm in diameter. They have a waxy appearance.

A patch test with tuberculin elicited a negative reaction. A roentgenologic examination of the chest did not show evidence of pulmonary tuberculosis.

The biopsy slide showed numerous epithelioid cells, a few plasma cells and an occasional Langhans giant cell. These cellular elements together with lymphocytes formed an infiltration of the dermis, presenting a picture consistent with granuloma annulare.

## DISCUSSION

MAJOR EVERETT R SEALS, M C, A U S (by invitation) Has any one followed granuloma annulare without any treatment long enough to determine the duration of the disease? Will the skin clear spontaneously after a time?

DR SAMUEL AYRES JR I do not think that I have ever followed granuloma annulare without treatment over a long period, but I have seen cases in which the eruptions have been present for periods of months to several years, and I know that cases in which the disease has lasted for years have been reported in the literature. This particular type of eruption is uncommon and is not similar in its clinical appearance to the more familiar type that occurs in ring formation on the hand.

**A Case for Diagnosis (Pigmented Basal Cell Epithelioma or Melanoma?)**

Presented by DR JOHN D ROGERS

Mrs V K, a white woman aged 59, has a brownish black, slightly elevated, irregular dime-sized lesion on the right cheek. In the lower margin is a small firm elevated lesion about 3 mm in diameter which shows some telangiectasia over its surface. The nodular lesion is about eight weeks old. The flat pigmented area has been present for twenty years. There has been no change in the past three years. There has been no treatment.

## DISCUSSION

DR M E OBERMAYER I do not feel that the tumor is a melanoma, but I believe that the dark lesion is a hyperpigmented seborrheic wart, from which a basal cell epithelioma has developed. I suggest a punch biopsy of the two types of lesions present in this area. Then let the therapeutic measures indicated by the microscopic aspects be followed.

DR SAMUEL AYRES JR I think that the members could argue at length and still have diverse opinions, but it seems to me that since this person has had a black lesion all her life and since some growth has recently taken place in that area every precaution should be taken. I do not see what objection there is to excising the entire area with a cutting cautery. There is no point in taking

specimens for biopsy here and there. It would not disfigure the patient's face to have the entire lesion taken out. I cannot understand why it would make any difference if procaine hydrochloride were injected around the infected area. Using the infiltration method of inducing anesthesia could make no difference, one way or another.

DR H P JACOBSON. On clinical grounds, I question the diagnosis of basal cell epithelioma. According to the patient's history, she has had the pigmented patch on the temple for at least twenty years. It is a sharply margined, non-elevated, deeply pigmented, irregularly shaped plaque. Extending from the lower border is a hemispheric nonpigmented nodule, approximately 1 cm in diameter. This is of recent origin. The morphologic picture, together with the clinical history, suggests a diagnosis of melanotic nevus and amelanotic melanoma. The therapeutic indications are definite. I cannot stress too emphatically the need for radical management of cases such as this. I have had the misfortune to see many tragedies resulting from conservative treatment of melanotic lesions, and, unfortunately, some of these tragedies have resulted from conservative treatment on the part of dermatologists. Some of the members are naturally much concerned with cosmetic results. In the treatment of malignant lesions, however, such considerations, in my opinion, are entirely unjustified. The only desideratum, which should be the dermatologist's guide, must be the destruction of the malignant lesion plus a safe zone of healthy tissue surrounding it. Melanotic malignant growths are radioresistant. The only logical and safe therapy requires radical surgical removal with the actual cautery under general anesthesia. I am opposed to infiltration anesthesia in cautery excision of these lesions.

DR J WALTER WILSON. I did see the case Dr Jacobson refers to, but I should like to go on record as believing that procaine anesthesia is not harmful.

DR W H GOECKERMAN. I think that Dr Jacobson is probably too much inclined to castigate the dermatologist. Every dermatologist worthy of the name is fully cognizant of the vicious character of certain pigmented lesions. While the detailed approach in treatment may vary somewhat, the aim is certainly to eradicate drastically any pigmented lesion that has the possibility of becoming a melanoma. On the other hand, I, too, feel that it is difficult clinically to be sure whether or not a pigmented lesion is already a melanoma if there is as yet no definite clinical evidence of growth. One of my colleagues, with much experience in the field of cancer, emphasizes this feature by saying that in his opinion if the Cohnheim theory of misplaced cells applies to any form of cancer it does so in the case of lesions that become melanomas. In fact, he feels that all of them are definitely malignant, even when not active. It is certainly wise, therefore, to approach any pigmented lesion with all possible caution.

NOTE.—A later report on a biopsy specimen from the lesion showed it to be a malignant lesion—a melanoma.

#### **Liquefying Nodular Panniculitis** Presented by DR SAMUEL AYRES JR

G C, a white woman aged 49, approximately three years ago had about fourteen lesions similar to the present ones. Just prior to the onset of the present lesions she lost almost 35 pounds (16 Kg) and had periods of nausea lasting for several days. Such an attack usually came just before the onset of a new lesion. She was free of lesions for one year until four months ago, when the present group began to develop. The first of these was on the right arm. All lesions follow a similar course. At first the patient feels a deep, slightly tender, thick, round lump which seems to be in the subcutaneous tissue. Nothing is visible. The process gradually enlarges and reaches the surface, forming a dull red elevation. This becomes fluctuant, breaks down, discharges and finally heals, leaving a depressed soft scar.

On the lateral surface of the right arm there is a new lesion, a slightly fluctuant, oval, brownish pink area, about 1 cm in diameter. Surrounding it

is a deeply infiltrated area, apparently involving the subcutaneous tissue. A similar lesion is on the lateral surface of the right thigh. It is an area of infiltration, about the size of a dime, which is not discolored and is only slightly elevated. Close to this is a pitted scar, also about 1 cm. in diameter. On the anterior surface of each shoulder and over the buttocks and the posterior surfaces of the thighs are numerous dime-sized depressed soft scars.

A tuberculin patch test was faintly positive after five days.

#### DISCUSSION

DR H. P. JACOBSON: I agree fully with the opinion expressed by Dr. Ayres. The differential diagnosis in this case rests between three possibilities: (1) the diagnosis as presented, (2) subcutaneous fibromas and (3) sarcoids. Subcutaneous fibromas and sarcoids usually show no tendency to suppurate. The presenting lesions, in contrast, show evidence of suppuration, followed by healed depressed scar formations.

DR W. H. GOECKERMAN: I should like to suggest the diagnosis of erythema induratum. Bazin emphasized in his original paper describing the disease that not all lesions of erythema induratum become necrotic and that these lesions need not necessarily predominate on the legs. My clinical experience agrees with this. Often too much emphasis is laid on the necrotic lesions occurring on the calf. A biopsy should be of help, although even it may not clearly distinguish between liquefying nodular panniculitis and erythema induratum.

DR SAMUEL AYRES JR.: In checking over the literature, I found that a case was reported by Dr. Bertram Schaffer in the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY* (38:535, 1938). At that time he expressed the opinion that it was a rather new entity, and he differentiates it from the relapsing febrile non-suppurative panniculitis (Weber-Christian syndrome). The lesions do not suppurate. In his case there was relatively little fever and at times none at all. Nearly all the lesions suppurated. One should also consider tuberculous gumma. The lesions in such cases are more chronic in their ulcerative phase. In this case, every individual lesion takes three or four months, after the time it is first palpated, to come to the surface and suppurate. Then it heals rapidly and is followed by a depressed scar as if some destruction of the underlying fatty tissue had taken place.

#### Anetoderma Erythematosum of Jadassohn (Dermatitis Maculosa Atrophicans). Presented by DR. M. E. OBERMAYER

H. F., a woman aged 32, has a healed tuberculous pulmonary lesion, diagnosed by roentgenologic examination when she was 19. She had a complete hysterectomy four years ago. The present cutaneous lesions began when the patient was 6 years old, after tonsillectomy. The first lesions were on her neck. One by one they came for a period of two years. The present "marks" have remained unchanged. No new lesions came until two years ago. Then they began to appear on chest, back, arms and legs. At first they were red, and gradually they underwent a scarlike change.

Individual lesions vary from 5 to 15 mm. in diameter. They are irregularly distributed on both sides of the neck and over the sternum, the extensor surfaces of the arms, the flexor surfaces of the forearms, the lower part of the back and the extensor surfaces of the thighs. The newer lesions are slightly erythematous, while the older ones are whitish and show a cigaret-paper-like wrinkling. The macules on the neck are distinctly depressed and arranged with their long axes in the direction of the lines of cleavage of the skin. Most of the lesions on the forearms are slightly elevated, soft and compressible, so that a hernia-like impression is gained from palpation.

The Kolmer and Kahn reactions of the blood were negative.

A biopsy specimen from one of the most recent erythematous macules on the right thigh showed an epidermis of normal thickness, with a fluffy corneal

layer and an absence of the rete processes. The corium was edematous, and the nuclei of the connective tissue cells were increased in number and size. The blood vessels were dilated, and a moderate amount of perivascular lymphocytic infiltration was present. The connective tissue fibers appeared somewhat homogenized. They were irregularly arranged and took the stain poorly. Sebaceous glands, sweat glands and lanugo hairs were normal.

## DISCUSSION

DR HAL E. FREEMAN. This eruption apparently is what I call a primary macular atrophy of the skin as opposed to secondary atrophies which follow other processes.

DR M. E. OBERMAYER. I agree with Dr. Freeman that this rare disease belongs to the group of primary macular atrophies, for, although the beginning of the process is of an inflammatory nature, the inflammation is an inherent part of the entity, and the atrophy does not follow an inflammatory process of a different kind. The interesting feature of anetoderma erythematosum is its characteristic course, which is made up of three stages, the initial erythematous macular stage, the erythematous annular stage with central atrophy and the final atrophic stage with the herma-like development. Another little known feature of the disease is the fact that the consistency of some of the herma-like lesions is caused by the formation of fatty tissue in the dermis. This eventually replaces the degenerated connective tissue fibers.

#### A Case for Diagnosis (Maculosquamous Eruption Resembling Lupus Erythematosus?) Presented by DR M. E. OBERMAYER

J. M., a white man aged 35, had an eruption soon after birth. The first lesions were two small brown "spots," which gradually enlarged, over many years. A few new lesions formed. Since he was 18 the process has remained stationary. The only subjective symptom has been an occasional slight itching.

There were about five erythematous plaques, measuring 1 to 2 cm. in diameter. They have irregular contours and a surface which has fine scales. The lesions are almost level with the skin. There is no sign of atrophy.

The biopsy specimen showed a thin epidermis, which varied in thickness. The irregular stratum mucosum had intercellular and intracellular edema and bulging rete pegs. The basal cell layer was intact. There was follicular plugging as well as slight parakeratosis. The dermis appeared filled with large lymph spaces and abnormally dilated blood vessels. A diffuse lymphocytic infiltrate was present all through the middle and the upper parts of the dermis where it blended with the epidermis. Many adenomatous sebaceous glands were present all through the dermis, the sweat glands and the subcutaneous tissue were normal.

## DISCUSSION

DR PAUL D. FOSTER. It is unusual to see a lesion of this type remain for such a long time. Clinically and microscopically the diagnosis of lupus erythematosus must be made. If the history is true, this patient is the youngest person with lupus erythematosus I have ever seen.

DR W. H. GOECKERMAN. I want to support Dr. Obermayer unhesitatingly in his suspicion of lupus erythematosus. The history may be disregarded. The clinical appearance is typical of lupus erythematosus, and with the supporting evidence in the microscopic picture I think that one need not hesitate in making that diagnosis.

DR SAMUEL AYRES JR. The patient said that he had had the lesions all his life. They must be nevi of some sort.

DR M. E. OBERMAYER. This case was presented "for diagnosis" in order not to bias the judgment of the members. I think that the clinical appearance of the lesions as well as the microscopic aspects point toward a diagnosis of chronic

discoid lupus erythematosus Yet, the course of the disease is most unusual It developed right after birth, evolved extremely slowly and then remained stationary for almost twenty years without producing definite clinical atrophy This behavior, together with the unilateral localization, made me consider an atypical form of nevus unius lateris

**A Case for Diagnosis (Contact Dermatitis?)** Presented by DR CLEMENT E COUNTER

D A, a white man aged 28, has had hives recurrently three times a year since he can remember There has been no urticaria in the last ten months The present eruption began about eight months ago It has been persistent ever since There have been some fading and some recurring, but given papules persist, even though they are redder at some times than at other times

The patient's general appearance is excellent The red papular eruption is distributed over a limited area around the hips In fact, papules are found only on the area covered by bathing trunks and on the medial surfaces of the arms Individual lesions are smooth and red and raised about 1 mm above the skin All lesions are discrete They average 3 mm in diameter

The biopsy specimen showed some perivascular round cell infiltration, evidencing a nonspecific inflammatory reaction There was an occasional mast cell

Ultraviolet rays have been used in mild erythema doses

DISCUSSION

DR H P JACOBSON The eruption is peculiarly limited around the hips to the area corresponding to the borders of his shorts I am inclined to think that it might be a contact dermatitis, either from the washing soap or the fabric of his underwear

DR W H GOECKERMAN I think that this eruption is urticaria papulosa If rubbed, the lesions become turgescient The patient has had urticaria The clinical picture is rather typical of that special kind of urticaria

DR M E OBERMAYER I am certain that this case is one of papular urticaria The presence of small vesicles on the top of some of the lesions makes it likely that the eruption is the type of papular urticaria known as strophulus

**A Case for Diagnosis (Lichen Planus?)** Presented by DR IRVING BANCROFT

V W, a Negro woman aged 32, three years ago began to have an itching eruption under her arms The same eruption appeared under the chin and on the back of the neck about two years ago Similar lesions developed on the medial sides of the arms about two years ago

The patient is obese There are hyperpigmented areas under the arms Excoriations are present In both axillary areas are finely furrowed and scattered papules There are also areas of lichenified scattered papules on the front and on the back of the neck The right elbow and both forearms have similar areas Hyperpigmentation is present in the older eruptions

Various ointments have been used locally, and bismuth subsalicylate in oil has been given intramuscularly

The Wassermann reaction of the blood was negative No fungous elements were demonstrated by direct microscopic examination of scales The biopsy specimen showed only round cell infiltration and other signs of nonspecific chronic inflammatory process

DISCUSSION

DR H C L LINDSAY The lesions on this patient do not look like those of lichen planus, but they do resemble patches of neurodermatitis

DR M E OBERMAYER The disease is more likely to be lichen chronicus simplex than lichen planus Differentiation in a dark-skinned person is not possible without biopsy



MAJOR EVERETT R SEALS, M C, A U S (by invitation) That is something readily seen in Houston, Tex. It is almost always found in Negroes. It is called neurodermatitis. It does not respond to any kind of treatment. It lasts more or less all the year around, but it is worse in the summer. Sweating is a factor in producing it.

#### **Urticaria Pigmentosa of Bullous Type** Presented by DR PAUL D FOSTER

S A is a girl 4 months old and is the only child. Her parents are well. The eruption has existed since birth. The reddish marks develop "blisters." When a "blister" breaks, the erythematous lesion remains. She has these lesions on the extremities, the body and the head. Apparently they cause no pain.

The baby's general appearance is healthy and well nourished. The lesions are in multiple areas on the body, the legs, the arms and the head. They are about 2 cm in diameter and irregularly round. All are pigmented a dark brown. The surfaces of the lesions have prominent follicular openings, producing the appearance of an orange peel. Some lesions have tense bullae present.

The biopsy specimen showed a thinned epidermis and an infiltration or replacement of the cutis by cells which were suggestive of nevus cells. The pigment was heaviest just at the basal layer of the epidermis.

#### DISCUSSION

DR PAUL D FOSTER The slide is strongly suggestive of a nevus, and the fact that the child was born with this disease strongly suggests the diagnosis of a nevus. It is the first case of this type that I have ever seen.

DR M E OBERMAYER Vesicle and bulla formation in cases of urticaria pigmentosa is extremely rare. Yet there is no reason for denying the possibility of bulla formation in any case of inflammatory dermatosis when the exudative process happens to be of an unusually high degree. I think that this child has a bullous form of urticaria pigmentosa.

DR H P JACOBSON The lesions presented by this child are peculiar tumor masses, which I have never seen. I have never observed such lesions in connection with urticaria pigmentosa. It is possible that these are lymphangiomas, associated with intense inflammatory cellular reactions.

#### **Keratosis Palmaris et Plantaris** Presented by DR SAMUEL AYRES JR

C B, a white child aged 9 years, has had an eruption for five years. At first only two fingers were involved. Later the disease extended to include the palms and the soles, and it has been persistent. No other member of her family has similar thickening of the palms and the soles.

The eruption is limited to the palms and the soles except for slight involvement on the anterior aspects of the ankles, the knees and the elbows. One year ago her feet were so badly broken out that it was necessary for her father to carry her into the office, and at that time the palms and the soles were extremely hyperkeratotic. Greater thickness was present on the backs and the medial aspects of the heels. With regard to the palms, the eruption was particularly bad on the tips of the fingers and on the hypothenar prominence. There was fissuring. Areas on the ankles, the knees and the elbows were less thickened. They were slightly erythematous, dry and scaly. There were ill defined dryness and roughness on the arms and the legs, with slight follicular hyperkeratosis. The hair on the forearms near the elbows is longer than that usually seen on children's extremities.

Normal amounts of nonprotein nitrogen and uric acid were present in the blood. No fungous elements were present in scrapings from plantar and palmar lesions.

Vitamin A has been given for the last year. During part of that time 150,000 units was given daily. Sixteen roentgen irradiations were given at weekly intervals.

Seventy-five roentgens was given to each lesion at each treatment. Local medications have included ointments containing juniper tar, salicylic acid, anthralin ointment and simple bland creams. The eruption has improved, but the hyperkeratosis continues.

## DISCUSSION

DR MILTON GOLDMAN (by invitation) I was interested in the possible functional nature of this eruption. The aunt and the grandmother on the maternal side had asthma. The mother recently had eczema. I thought of the possibility of a functional dermatosis.

DR M E OBERMAYER I agree with Dr Goldman. Keratosis plantaris is hardly ever present in the form of sharply circumscribed plaques. I have never seen a case in which such plaques were located also at the sides of the feet. The disease is more likely to be a hyperkeratotic form of dry neurodermatitis.

DR RICHARD L SAUNDERS (by invitation) This case impressed me as one of psoriasis of the palms and the soles.

DR A FLETCHER HALL I agree with the diagnosis of psoriasis. Biopsy would prove it.

**Neural Leprosy (Maculoanesthetic Form?)** Presented by DR MOLLEURUS COUPERUS

E B is a young Mexican woman aged 19. Her father died of alcoholism. Her sisters and her mother are living and well. None of her family or near relatives have had any cutaneous disease. She entered the United States one year ago. Four years ago a small red spot appeared on the right leg. Its enlargement has been gradual since then. A few small red spots have appeared on the other leg and the thigh during the past month. The patient has noticed that there is no sensation of pain in certain parts of the large area on the leg when the area is scratched. She is underweight.

On the outer aspect of the right leg, covering the lower two thirds and almost encircling the leg in the middle, is an erythematous plaque which is macular in type except at the periphery, where there is a slight elevation suggesting minute nodules. The entire lesion is slightly scaly, and there is atrophy in the central part of the patch. There is no sensation of touch or pain in this area. Outside the large patch as well as in a few areas on the trunk and on the opposite leg there are pea-sized erythematous macular areas. Some of these are hypersensitive, and some are anesthetic.

The Wassermann reaction of the blood was negative. *Mycobacterium leprae* was not found either in repeated nasal smears or in repeated smears of material obtained by puncture from the lesion on the leg.

The biopsy specimen showed thinning of the epidermis. In the upper part of the cutis there was considerable dilatation of the blood vessels, and here, as well as through the entire cutis, there were focal aggregates of epithelioid cells associated with small round cells and fibroblasts. Some of the infiltrate surrounded nerve fibers.

## DISCUSSION

DR M E OBERMAYER I agree with the diagnosis, though I had no opportunity to study the section. That the patient came from Sinaloa is significant because that state has the highest incidence of leprosy in Mexico. I should like to perform the Mitsuda-Rost test on this patient. As I had the opportunity to observe during my recent visit to Mexico City, the prognostic significance of this test is paramount. A positive reaction indicates a satisfactory allergic response and is encountered in practically all cases of tuberculoid lepra. The course of the disease will remain relatively benign, and specific therapy is apt to bring improvement. A negative reaction indicates a lack of allergic response and is encountered in the lepromatous forms of the disease. The test is performed by intracutaneous injection of an antigen derived from maceration of tissue rich in

lepra bacilli and is read in the same way as a tuberculin test. Dr Fernando Latapi, professor of dermatology at the National University of Mexico, not only demonstrated the Mitsuda-Rost test for my benefit but has also supplied me with antigen. From what I have learned in Mexico it may be said that a correct diagnostic interpretation of a case of leprosy without the aid of the Mitsuda-Rost and histamine tests is a thing of the past.

DR HAL E. FREEMAN: In the few cases of leprosy that I have seen, erythema has not been present in the anesthetic areas. Just looking at the process in this patient, one would think of the clinical picture of Kaposi's idiopathic hemorrhagic sarcoma.

DR SAMUEL AYRES JR: Were Hansen's bacilli found in the tissue?

DR MOLLEURUS COUPERUS: This form of leprosy often shows no Hansen's bacilli in biopsy specimens or in material obtained by superficial punctures of the skin. I do not believe that any other diagnosis is possible in this case. The erythema is greatest near the advancing border of the lesion, while in the center it is much less. This is not uncommon. From a clinical standpoint this form of leprosy has a fairly good prognosis with modern therapy. I shall be happy to have Dr Obermayer perform a lepromin test on this patient.

NOTE—A histamine test of this patient failed to elicit an erythematous flare in the area of the cutaneous lesion but produced such erythema elsewhere. Dr Obermayer performed the Mitsuda-Rost (lepromin) test, which elicited a positive reaction.

#### Localized Hyperhidrosis Presented by DR SAMUEL AYRES JR

R. S., a man aged 59, has had hay fever most of his life during the summer.

His hyperhidrosis began about thirty-five years ago, after an illness involving an appendectomy and at the same time the incision of an abscess near the angle of the right jaw. Ever since that time his right cheek has broken out with profuse perspiration a few minutes after eating. Such foods as chocolate cake particularly stimulate this perspiration. The attack usually comes on within ten minutes after eating and persists for five to fifteen minutes. The perspiration drops off his chin, necessitating the use of a handkerchief.

The patient ate a lunch just before being observed at the clinical presentation. Much clear fluid accumulated on the right cheek in a defined round area about 6 cm in diameter. Enough fluid accumulated to run down and drip off the chin. The flow of the fluid stopped in five minutes. Only slight erythema of the right cheek was left to show where the fluid had come from.

Positive reactions of the skin were not produced by any of the one hundred and fifty food pollen extracts tested.

#### DISCUSSION

DR PAUL FOSTER: This case represents a vasomotor imbalance brought on after an operation for a deep abscess thirty-five years ago. At that time a large incision was made that went deep into his neck, and immediately afterward the right side of his face started to perspire. I have seen 2 cases in which the sympathetic cervical ganglions had been anesthetized with procaine. In each instance there was localized increase of perspiration like that present in this case.

DR ANKER JENSEN: I believe that this man has some extra parotid tissue close to the surface of the skin. His condition may be analogous to endometriosis.

DR SAMUEL AYRES JR: The fluid has the appearance and the consistency of perspiration. This sweating develops only after the patient has eaten, and especially after he has eaten rich food. One of my classmates had a similar hyperhidrosis when eating peanuts or chocolate. On scratch tests this patient did not show hypersensitivity to food proteins, but he has had hay fever for many years, suggesting an allergic background. The discomfort comes from the necessity of mopping his face with a cloth after every time he eats.

## MANHATTAN DERMATOLOGIC SOCIETY

George M Lewis, M D , *President*Wilbert Sachs, M D , *Secretary*

Feb 13, 1945

**A Case for Diagnosis (Eruption of Chest and Back, Aggravated by Sunlight)** Presented by DR JACK WOLF

R M, a woman aged 24, is presented with an eruption of approximately four years' duration, which began in the presternal region and gradually spread peripherally until it reached its present size. Satellite lesions have continued to appear. The only relevant observation that the patient has made is that the eruption becomes more acute on exposure to the sun but that it does not necessarily spread as a result of such exposure.

On examination the patient presents a diffuse mottled erythematous eruption, forming a more or less reticulated pattern and extending from the supraclavicular regions down to the inframammary area. Laterally it extends as far as the midclavicular line. The individual lesion is barely perceptible to the touch, and the elevation can be seen only when observed at the proper angle.

A piece of tissue removed from one of the more prominent lesions revealed only a moderate interstitial and parenchymatous edema in the upper and middle parts of the corium, with superficial dilatation of the vessels. No histologic diagnosis could be made.

## DISCUSSION

DR FRED WISE I suggest a diagnosis of atypical seborrheic dermatitis, and I should use resorcinol lotion as a therapeutic test.

DR HERMAN SHARLIT I agree with the suggestion of Dr Wise.

DR MAX SCHEER I, too, agree with the diagnosis, especially on account of the lesions between the shoulder blades, which look much like seborrheic dermatitis to me.

DR DAVID BLOOM This patient shows tiny papules in linear arrangement, which I have seen in a case of ectodermal dysplasia of the anhidrotic type and which has also been described by MacKee in his case. The lesions were located on the neck in those cases and were supposed to be due to degeneration of sebaceous glands. I do not know whether these lesions have any connection with the eruption for which the patient was presented.

**A Case for Diagnosis (Poikiloderma Vasculare Atrophicans?)** Presented by DR FRED WISE

F S, a woman aged 26, was referred by Dr Harold N Cole, of Cleveland, with an eruption of the body which she has had practically all her life. The family history is essentially noncontributory. The patient states that she used to perspire on her face and her back and under her arms and that she still perspires on her face and under her arms. She notes some perspiration on her palms during warm weather. She says that in hot weather she is uncomfortable and that her face gets flushed, although she does do some work.

An examination revealed an eruption that is most extensive on the arms and on the legs down to below the knees, being almost confluent in those areas, and even up onto the buttocks, with large, fairly well circumscribed areas on the trunk. There are also confluent areas on the neck. There are two types of lesions, the one in the form of macular pigmented areas and the other in that of erythematous retiform areas with telangiectasia, atrophy and scaling. Some fine telangiectases are present on the cheeks. The mucous membranes, the nails and the teeth are apparently normal.

A roentgenologic examination revealed that the chest is normal. The basal metabolic rate was —7 per cent. The blood calcium was 12 mg and the blood phosphorus 3.5 mg per hundred cubic centimeters. At the time of her examination vitamin C was 0.3 mg and plasma cholesterol 221 mg per hundred cubic centimeters, and the hemogram was perfectly normal, with a white blood cell count of 7,500.

A histologic examination showed considerable keratinization of the epithelium, with epithelial pegs entirely absent. The basement membrane of the epithelium was intact. In the upper portion of the dermis was a considerable infiltration of lymphocytes and large round cells. There was also some collagenous degeneration of the connective tissue. Hair follicles and sweat glands were found in the deeper portion of the dermis. There were scattered collections of inflammatory cells similar to those already mentioned, especially around vessels. The elastic tissue appeared fragmented.

#### DISCUSSION

DR HERMAN SHARLIT: What is the modern treatment?

DR GIRSCH D. ASTRACHAN: This patient presented a pronounced diminution of vitamin C in the blood, the values being less than half of normal. That might provide a basis for therapy.

DR WILBERT SACHS: I believe that all the members agree with the diagnosis. Some of these extensive eruptions eventuate into mycosis fungoides.

DR MAX D. SCHEER: I think that a patient was reported on years ago in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY as having poikiloderma vasculare atrophicans and dying later of mycosis fungoides.

DR WILBERT SACHS: That is not the only case, others have been reported.

DR DAVID BLOOM: In the past few years I have had under observation several patients with this type of eruption. My impression is that it is due to a vascular disturbance of congenital origin. I am inclined to consider the occasional association with mycosis fungoides as coincidental.

#### Koilonychia Presented by DR ANTHONY C. CIPOLLARO

E. R., a nurse aged 46, born in the United States, was the subject of an article which appeared years ago in the *New York State Journal of Medicine* (30:380 [April] 1930). She is now presented to show that the koilonychia has not changed in any fundamental way since then. She has had it since birth, and her mother and sister have a similar anomaly. While the patient was on duty in the operating room, contact with strong antiseptic solutions made the disease worse and caused pain. She is presented not only because this disease is unusual but also to reaffirm the fact that hereditary factors are the most pronounced in the causation of koilonychia.

#### DISCUSSION

DR DAVID BLOOM: Koilonychia belongs to the nail dystrophies which are inherited according to a dominant mode.

DR FRED WISE: It is an interesting observation that about five years ago an article was published in which it was stated that in practically every case the anomaly is associated with achylia gastrica. Dr Cipollaro tells me that everything points against that probability in this case, although no analysis of the gastric content has been made. The fact that other members of the family have the same trouble suggests inherited disease. That angle should be investigated.

DR HERMAN SHARLIT: The fact that a hereditary factor is involved does not mean that there is no remedy.

DR ANTHONY C. CIPOLLARO: About 35 per cent of the cases of koilonychia reported in the literature have heredity and occupation as assignable causes. In about 30 per cent there were associated diseases. In none of the cases reported

were there any internal disturbances other than those which were coincidental I did not perform an analysis of the gastric content in this case as there was no indication for it in a perfectly healthy patient. But I did determine the basal metabolic rate and made a blood count, and I searched for foci of infection or evidence of other congenital anomalies, without result.

**A Case for Diagnosis (Toxic Erythema? Lupus Erythematosus?)** Presented by DR DAVID BLOOM

M Q, a woman aged 28, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov 1, 1944, complaining of an eruption of seven years' duration. At that time the patient presented underneath the left breast a well defined dusky red plaque, semilunar in shape, in which the follicular openings were distinct as dark red spots. On the chest, over each supraclavicular region and on the back to the right of the left scapula there were plaques which consisted of ill defined, slightly raised, light red, edematous papules. After a few injections of bismuth subsalicylate the eruption improved considerably. The plaques became lighter, and some of them cleared almost entirely.

The patient now presents underneath the left breast a plaque which is light red, with follicular openings which are distinctly seen as pits. On the chest the plaques, consisting of light red edematous papules, are seen with difficulty, but in the supraclavicular regions the follicular openings are conspicuous and appear as being depressed. On the back the plaque can be distinguished only with difficulty.

The past and family histories were essentially noncontributory.

The urine and the blood count were normal. Biopsy revealed merely edema. The Wassermann reaction was negative.

DISCUSSION

DR FRED WISE: There is no evidence of any kind in support of the diagnosis of lupus erythematosus. In the Jadassohn Handbuch there are descriptions of various inflammatory follicular diseases associated with pitted atrophy of the follicular orifices.

DR MAURICE J COSTELLO: The follicular atrophy is of course the end result of the inflammation which preceded it. I observed for some time at Bellevue Hospital a patient, later reported on by Dr Combes, who presented a picture somewhat similar to this, and I came to the conclusion that the eruption was an atrophic follicular form of lichen planus. I do not think that the history is consistent, but the eruption strongly resembled it clinically.

DR DAVID BLOOM: The patient is presented for two reasons: first, for the remarkable improvement of the eruption which suggests a toxic erythema and, secondly, for the peculiar enlargement of the follicular ostiums.

**A Case for Diagnosis (Vitamin C Deficiency? Schamberg's Disease?).** Presented by DR GIRSCH D ASTRACHAN

Z L, a white boy aged 14, born in the United States, came to my office on Nov 10, 1944, presenting an eruption on both legs and thighs of seven months' duration. The eruption began with a few lesions and spread gradually. It was composed of many scattered and closely set papular and macular lesions, many of which were purpuric in character, others being red to light brown. The patient complained of slow healing of the wounds and frequent infections of the skin. He was advised to drink large quantities of orange and tomato juices. Calcium gluconate and a proprietary exsiccated ferrous sulfate were prescribed. The eruption has improved during the last two months.

The patient now presents on both legs and ankles and the lower parts of the thighs an eruption composed of well defined, irregularly shaped lesions, varying

in size from that of a pinhead to that of a quarter, most of which are macular in character, others elevated and somewhat infiltrated. The color varies from yellowish brown to reddish brown. Several scars and a few lesions suggestive of slight atrophy are present on both legs.

A blood count on Oct. 23, 1944 showed 9,600 leukocytes, of which 42 per cent were neutrophils, 51 per cent lymphocytes and 6 per cent monocytes. The erythrocyte count was 3,860,000, the hemoglobin content 81 per cent and the platelet count 190,000. The bleeding time was three minutes and fifteen seconds, and the coagulation time was sixteen minutes. The vitamin C content of the blood plasma was 0.34 mg per hundred cubic centimeters. The Wassermann and Kahn reactions of the blood were negative. The sedimentation rate was normal. The icterus index was 7.5 units. The uric acid was 3.8 mg per hundred cubic centimeters, dextrose, 75 mg.

Histologic examination of one of the lesions taken from the leg suggested the diagnosis of hemostatic dermatitis ("could possibly fit in with Schamberg's but not with Majocchi's disease" [Dr Sachs]). Throughout the middle and upper parts of the cutis the vessels were somewhat dilated and the walls thickened. There was a moderate amount of telangiectasia. There was a focal small round and wandering connective tissue cell infiltration. Throughout the remainder of the cutis was a diffuse sparse fibroblast cell infiltration. The overlying epidermis was somewhat edematous in the lower portion, but otherwise it showed no important change.

#### DISCUSSION

DR ANTHONY C. CIPOLLARO: I do not believe that the patient suffers from a drug eruption. It is a purpuric eruption of some type, the exact nature of which I am unable to determine. Whenever I see a case of this type I have difficulty in differentiating between Schamberg's and Majocchi's diseases and purpura simplex. The vitamin C determination is a good thing to have, though I do not know how much significance it has from the standpoint of causation. If the vitamin C value is below normal, one can increase the intake, but I have not seen any effect of that on an eruption of this type.

DR FRED WISE: I have never seen a clinical picture corresponding to this one. The variability of the lesions and of their size seem to me most unusual. One disease which could be eliminated is Schamberg's, as there is absence of hyperpigmentation in these lesions. From a distance the eruption simulates Majocchi's disease, but the histologic report fails to confirm the diagnosis since sacculization, hyalinization of the vessels and other criteria are lacking. The diagnosis seems to lie between purpura and dermatitis hemostatica. I see no reason why a healthy young boy with no signs of circulatory disturbances should have dermatitis hemostatica, and I therefore come to the conclusion that the eruption is an aberrant or atypical form of purpura.

DR DAVID BLOOM: I should like to suggest the diagnosis of pigmented purpuric lichenoid dermatitis of Gougerot and Blum.

DR FRED WISE: That does not resemble this. There are pinhead papules, and they are so small that one has to search for them.

DR HERMAN SHARLIT: I suggest that some of the patient's blood be taken and hemolyzed and that the patient be given an intracutaneous injection of it. The blood on extravasation into the tissues may be causing a reaction *in situ*. This procedure may reveal such a status.

DR WILBERT SACHS: Of this whole group of diseases, the one that can be diagnosed with ease by microscopic means is Majocchi's disease. As Dr Wise said one must have hyalinization of vessels, sacculization and other changes in order to make a diagnosis of Majocchi's disease. The other three may be very similar. Surprisingly enough, there is little to be seen microscopically in purpura. Schamberg's disease is more of an inflammatory process, while dermatitis hemostatica

is a long-standing process with telangiectasia and even some fibrosis. One could certainly rule out Majocchi's disease in this case on the microscopic features. I favor a diagnosis of dermatitis hemostatica, or possibly Schamberg's disease.

DR GIRSCH D ASTRACHAN: When I first saw this patient he presented real purpura with many small and large macular and papular lesions, purplish in color. He complained of slow healing of any wounds, and of frequent infections. The eruption improved greatly after the administration of calcium by mouth and the intake of large quantities of orange and tomato juices. I cannot make a definite diagnosis, but I do not think that one is dealing with a case of dermatitis hemostatica, because of the youth of the patient and because he has no varicose veins or circulatory stasis. The eruption is probably caused by vitamin C deficiency, and I shall try large doses of ascorbic acid.

#### A Case for Diagnosis (Trichokryptomania?) Presented by DR HERMAN SHARLIT

M W, a girl aged 19, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb 9, 1945, complaining of thinning and poor growth of her hair. She said that about one year previously a small bald spot appeared on the vertex of the scalp, which soon extended to involve the whole anterior aspect. After four or five months the hairs returned but did not grow beyond  $1\frac{1}{2}$  to 2 inches (about 4 to 5 cm) in length.

At present the anterior aspect of the scalp and the parietal region show a thinning of the hair, which is not more than  $1\frac{1}{2}$  to 2 inches long. On the occipital and temporal regions the hair is normally thick and long.

The patient states that she has been treated by a commercial hair specialist, who advised her to brush her hair all day long. Recently she brushed her hair twice a day for ten minutes each time.

The past and the family histories are essentially irrelevant except that a younger brother is a mongolian idiot.

#### DISCUSSION

DR MAURICE J COSTELLO: I agree with the diagnosis. Sometimes a person will take instructions entirely too literally, and oftentimes merely rubs over small patches of the scalp, actually removing the hair by mechanical friction. These patients are of the hysterical type. In persons with an eruption such as this, which has persisted for ten years, I believe that other stigmas of hysteria could be demonstrated.

DR DAVID BLOOM: The diagnosis of trichokryptomania can be made by exclusion. The bizarre picture of very short hair on the anterior aspect of the scalp with perfectly normal hair on the rest of the scalp and the history of vigorous daily brushing of the hair, together with the normal appearance of the hair under the microscope—all this justifies the diagnosis.

DR FRED WISE: I do not agree with the diagnosis as presented, because of the uniformity of the alopecia and the absence of isolated patches resulting from recurrent plucking of the hairs on different areas of the scalp, as occurs in cases of genuine trichokryptomania in children. In this patient there is no evidence of a compulsion neurosis. I am more in favor of fragilitas crinium or some similar abnormality.

DR WILBERT SACHS: Why is it that after so many years of rubbing the scalp, the hair is broken off and not lost? Years ago Dr Wise reported a case of neurodermatitis of the forearms with complete alopecia.

DR THOMAS N GRAHAM: I think the fact that the involvement is so sharply outlined probably indicates that the patient used a brush only in that particular area. There is no loss of hair on the sides or the back of the scalp. These aspects would fit in well with a diagnosis of trichokryptomania.



**Leiomyoma** Presented by DR HERMAN SHARLIT

R C, a woman aged 28, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complaining of an eruption on the right side of the chest of six years' duration

On the right side of the chest above the breast there is an eruption of nodules which involve an area the size of a palm. The nodules are mostly lentil sized and reddish and are raised above the level of the skin. There are three pea-sized nodules which are extremely tender to pressure.

Biopsy confirmed the diagnosis of leiomyoma.

## DISCUSSION

There was no discussion of this case.

**Sarcoidosis** Presented by DR DAVID BLOOM

P H, a Negro woman aged 30, came to the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan 17, 1945, complaining of an eruption on the face and the neck of four years' duration. Her past and family histories were irrelevant except that from 1942 to 1944 she received intravenous and intramuscular injections at New York City Hospital, Welfare Island, in spite of a negative Wassermann reaction of the blood.

The eruption consists of a variety of lesions. On the glabella, at the outer aspect of the right eyebrow and on the tip of the nose and the upper lip, there are raised soft plaques, dark red-brown in color. The ear lobes and the ears are similarly affected. On the upper and the lower eyelids, in the canthi of the eyes, in the nasolabial fold and in the angles of the mouth, there are small round and annular lesions and groups of small nodules. On the lateral and posterior aspects of the neck there are depigmented linear lesions and groups of nodules.

A general examination revealed slight enlargement of the lymph nodes and the liver.

The Wassermann and Kahn reactions of the blood were negative. The blood count revealed anemia with eosinophilia and relative lymphocytosis (hemoglobin, 65 per cent, erythrocytes, 3,900,000 and leukocytes, 6,100, with 34 per cent neutrophils, 8 per cent polymorphonuclear eosinophils, 1 per cent basophils, 12 per cent monocytes and 41 per cent lymphocytes, with an occasional atypical cell). The sedimentation rate was greatly increased (62 mm, instead of 15 mm, an hour). A roentgenogram of the chest showed considerable nodulation at the hilus of each lung with small lymphoid deposits in the central pulmonary field. The thickening extended and diminished toward the periphery. There was otherwise no evidence of recent parenchymatous infiltration. The central thickening and nodulation were such as might well be observed with sarcoidosis. Tuberculin in a dilution of 1:10,000 elicited a negative reaction. Biopsy confirmed the diagnosis of sarcoid.

## DISCUSSION

DR ANTHONY C CIPOLLARO: There are some interesting features in connection with this type of sarcoid. A patient, especially one of the Negro race, with so much evidence of the disease diagnosed as sarcoid, is a candidate for milary tuberculosis. I recall a husky, 6 foot (182 cm) Negro with nodular lesions scattered all over the body, diagnosed both clinically and histologically as sarcoid, who died a year or two later of milary tuberculosis.

DR MAURICE J COSTELLO: The roentgenographic picture of sarcoidosis closely resembles that of acute milary tuberculosis, and I would be better satisfied in those cases if the diagnosis were proved correct post mortem. It is almost impossible to distinguish roentgenographically between acute milary tuberculosis, carcinomatosis and pneumoconiosis.

DR DAVID BLOOM: My conception of this type of eruption, seen frequently in the Negro, is that it is an attenuated type of tuberculosis associated with a high

immunity Many of these patients get entirely well with supportive therapy and some without any therapy at all

### Pyoderma Treated with Penicillin Ointment Presented by DR GEORGE M LEWIS

H D, a white man aged 43, came to the New York Hospital on Nov 4, 1944, with a swollen, exudative, erythematous and pustular eruption of the fingers of both hands, more severe on the left hand A diagnosis of pyoderma was made

A similar eruption had been present in 1933 for over five months before it responded to roentgen ray therapy Cultures on blood agar revealed *Staphylococcus aureus* and hemolytic streptococci

Treatment at first consisted of wet dressings and applications of ammoniated mercury ointment There was some temporary improvement, with prompt relapse when treatment was discontinued Treatment with penicillin ointment (400 units per gram) was begun on January 29 The response was favorable and rapid

#### DISCUSSION

DR HERMAN SHARLIT What is the opinion of Dr Lewis as to the stability of penicillin in the ointment? I have heard conflicting reports On the other hand, there have been cases of sycosis presented in which the eruption was considered cured by this agent

DR MAURICE J COSTELLO I have heard that penicillin ointment remains stable for several months if kept in the refrigerator

DR THOMAS N GRAHAM I saw this patient several times, and I can vouch for the severity and persistence of the eruption It was treated by many other measures without benefit, and the favorable response to penicillin ointment was most striking

### NEW ENGLAND DERMATOLOGICAL SOCIETY

Jacob H Swartz, M D, *President*

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Feb 14, 1945

### Colloid Degeneration of the Skin Presented by DR JOSEPH GOODMAN, Boston

M R, an Irish housewife aged 62, presented a lesion of the forehead of four months' duration At the onset there was a small reddish papule This gradually increased in size, and similar lesions formed at its periphery

On the left side of the forehead, there is an area 2.5 cm in diameter consisting of yellowish translucent nodules 2 to 3 mm in diameter surrounded by flat yellowish macules which are 1 mm in diameter

The results of the examination of the blood and the urine were within normal limits The Kahn and Hinton reactions of the blood were negative Histologic sections confirmed the diagnosis of colloidal degeneration of the skin

#### DISCUSSION

DR WALTER F LEVER The slide showed considerable degeneration of the collagen and elastic fibers They were matted together into a structureless mass I think the appearance of the slide was consistent with the diagnosis of colloid degeneration of the skin

DR BERNARD APPEL It seems to me that it might be worth while to mention the clinical picture that one gets by looking at the lesions which at first glance present a pale orange-yellow color The translucence and the color of the lesions suggest a xanthomatous tumor It might be interesting to speculate on the relationship between the colors Here is a tumor which seen microscopically, contains

no cells which can be considered to be xanthomatous in nature, and yet the color is suggestive of a xanthomatous infiltration. The question arises as to the origin of this color. It might be of some value to try to explain the interesting physical character of the lesions.

**Lichen Planus Hypertrophicus** Presented by DR LEO KORETSKY, Chelsea, Mass

C F, a 50 year old white American housewife, presents pruritic lesions of the axillas, the neck and upper portions of the gluteal fold of one year's duration.

Scattered in the axillas and over the neck, there are shiny papular lesions and patches which have a deep purplish color. At the axillary portions bilaterally on the chest, there are crescent patches consisting of purplish and brown scaling lesions. There is a similar eruption in the upper portion of the gluteal fold.

Urinalysis on January 22 revealed fifteen hyaline and granular casts per high power field, on January 29 the results of an examination were within normal limits. The Hinton, Wassermann and Kahn reactions of the blood were negative. The histologic examination confirmed the diagnosis of lichen planus.

Two treatments with mercuric succinimide and one with bismarsen have produced no change in the lesions.

DISCUSSION

MAJOR EARL A GLICKLICH The lesions which were in the axillary fold gave me the impression that they looked somewhat like those I have been seeing among the military personnel. The multiple excoriations of the forearms did not resemble lichen planus. She is rather an obese woman, and I believe the same type of reaction can be seen in one who wears a tight brassiere from contact in that area, which with moisture may produce a contact dermatitis.

DR JACOB H SWARTZ There were lesions in the mouth which were typical of lichen planus.

DR FRANCIS M THURMON I thought the configuration of the lesions was a bit unusual for an out and out lichen planus. Certainly the color and the thickening of the lesions were suggestive of lichen planus, but when I looked at the microscopic section and saw the bandlike arrangement of infiltration it was typical of or consistent with lichen planus. I believe the greater part of the eruption was lichen planus, with possibly a superimposed dermatitis venenata.

**A Case for Diagnosis (Melanosis of the Face and Neck, Keratosis Follicularis?)** Presented by DR BERARD APPEL, Lynn, Mass

C S, a 28 year old white woman who is a brusher in a leather tannery, presents lesions of the face and neck of six months' duration. In May 1944 she started work filling bottles with glue which was thinned with carbon tetrachloride. In August the onset was marked by itching and the appearance of "bumps" and discoloration of the skin of the face and neck. By October her illness forced her to cease work.

Examination reveals uniform, closely placed macules in profuse and masklike distribution over forehead, cheeks, ram and neck. Their dark pinkish brown color produces a "dirty," pigmented appearance of the skin.

The results of the hematologic examination showed hemoglobin, 90 per cent, erythrocytes, 3,720,000, leukocytes, 6,100, and a normal differential count. With the exception of a greenish yellow reaction for sugar, the urinalysis was within normal limits. The Hinton reaction of the blood was negative. A biopsy specimen showed moderate acanthosis and a collection of pigment in the upper portion of the corium.

Treatment consisted of the oral administration of vitamin A and reduced iron.

DISCUSSION

DR JOHN G DOWNING I saw a girl in my office about two months ago who had a similar eruption. She had the lesions on the face and light brown macules

around the waistline. She had nothing else. I took her into the Evans Memorial Hospital and studied her carefully. I thought at one time a pathologic condition was present in the liver, but nothing definite was found on which to base an etiologic factor. Biopsy was performed with the idea that the eruption might be an unusual type of lupus erythematosus of a pigmented nature which has been described. I thought it might be an unusual type of lichen planus. It is not my conception of the melanosis of Riehl as I saw it in Europe. It is not my idea of keratosis follicularis. I can only suggest negative evidence rather than positive.

DR FRANCIS M. THURMON: Except for the distribution of the pigmentation and the dirty brown appearance, the lesions on the face are suggestive of berlock dermatitis, which is due to the topical application of some photosensitizing substance. I believe in this instance, since this girl works as a brusher in a tannery, the dermatitis may have been caused by some substance with which she came in contact.

DR JOHN G. DOWNING: I should like to agree with Dr. Thurmon. The girl whom I observed was a welder, and of course she was exposed to the arc light and a certain amount of ultraviolet rays. The eruption on the waist was entirely different from the eruption on the face.

DR E. MYLES STANDISH: I asked the girl carefully about cosmetics and whether or not she used perfumes. She uses La Salle powder and rouge. The only contact she made in the factory was with glue and carbon tetrachloride. I thought the eruption looked like lichen planus. There was a definite shiny aspect to the flat-topped papules.

DR BERNARD APPEL: I took the opportunity of looking up something about melanosis, and there are a picture and a description in the *Corpus Iconum Morborum Cutaneorum* of the Budapest Congress of 1935. The picture, no. 4,465, depicts melanosis of Riehl. In that particular picture the lesions have more of a follicular distribution than this girl presented today. In that respect it is different. In respect, however, to all the cases that are described in that *Corpus Iconum*, particularly as to the relation of distribution of the exposed areas—areas which are obviously subject to photosensitization—I consider that this case resembles it. This case also resembles those described in the *Corpus Iconum* with respect to the color of the macules. Riehl himself had an interesting explanation of eruptions of this type, namely, that they are essentially a reaction of skin sensitized by sunlight. Practically all occur in women, and at one time Riehl felt that a dysvitaminosis was the basis of the sensitization. A man by the name of Baroni had an ingenious explanation. He reported a large number of cases and felt that the eruptions were due to face powder. The aniline dye in the face powder has a ring nucleus similar to that in tar derivatives which acts as in the cases which Riehl described in sensitizing the skin to the sun. He thought that in these cases the lesions were due to chemical sensitization rather than to dysvitaminosis. Histologically, this picture fits in with the description given by Riehl. There are some acanthosis and edema of the prickle cell layer. Collections of large granules of pigments obviously in clusters are present in the upper part of the corium. The pigment of the basal cell layer is less than expected. I think this probably is a case of melanosis of Riehl. Now, as to the question of the occupation of a brusher, it consists of placing the skins which have been completely tanned, dyed and finished into a machine consisting of two large revolving brushes which are made the same as the rollers of a wringer, only the fibers touch the skin lightly. Usually there is a suction device or hood ventilation that draws off the dust, but, even so, there is considerable dust around the machines. I have seen a number of patients who have had various dermatoses who are operators of brushing machines, and I have never seen anything like this eruption in any one in a leather factory. I think it will turn out to be a result of her having been sensitized to some cosmetic and the nature of it is melanosis of Riehl.

**A Case for Diagnosis (Parapsoriasis?)** Presented by DR ALFRED HOLLANDER, Springfield, Mass

M W, a 51 year old white man, presents a generalized eruption of nine months' duration. The onset was marked by a lesion 3 cm in diameter on the left side of the forehead, to which various ointments had been applied topically, including sulfanilamide for one day. The eruption gradually spread over the face and by October had extended over the whole body. At the time he was first seen, in December, a generalized dermatitis was present, in addition to the psoriasiform lesions. The acute dermatitis and the itching subsided with mild topical applications.

The eruption on the face, arms and thighs is retiform in character. Reddish yellow plaques with fine scales are seen on the neck, forearms, trunk and legs. Guttate lesions also are present on the trunk. Removal of the scales by scratching reveals punctate bleeding points.

Histologic examination showed parakeratosis, acanthosis and infiltration in the upper portion of the corium.

Treatment consisted of Aquaphor (an oycholesterol-petrolatum ointment), with 2 per cent salicylic acid topically and solution of potassium arsenite, U S P internally.

## DISCUSSION

DR GEORGE E MORRIS I believe this man has psoriasis rather than parapsoriasis. He has lesions on the penis, back and buttocks which are typical of psoriasis.

DR WALTER F LEVER I agree with Dr Morris.

DR JACOB H SWARTZ I think it is psoriasis, but I should like to add the fact that one should consider premycosis fungoides with mycosis fungoides later.

DR ALFRED HOLLANDER I have to admit that the histologic picture looks like psoriasis, but there are a few cases of parapsoriasis which show a picture which cannot be distinguished from psoriasis. When I saw the specimen, I considered the question of premycosis fungoides but in making a diagnosis I believe one has to consider the results of the treatment. *This man has not had any antipsoriatic treatment.* On the contrary, before I saw him, he was treated with many types of preparations, including ammoniated mercury, and he reacted with a generalized dermatitis. After that the lesions appeared again, as they are today. In my experience, parapsoriasis does not react at all to mercury or show a severe flare-up. Despite the rather typical histologic picture of psoriasis I think this is parapsoriasis.

**A Case for Diagnosis (Pseudopelade, Alopecia Cicatriza?)** Presented by DR BERNARD APPEL, Lynn, Mass

J McL, a white school boy aged 12, presents lesions of three years' duration involving the scalp and the posterior portion of the neck. The onset was marked by a lesion which developed on the posterior portion of the neck following chickenpox. The eruption has varied in intensity but at no time has there been complete remission.

Examination reveals an area of atrophic scarring 4 cm in diameter on the vertex of the scalp, the center portion of which presents a few hairs, while at the periphery there are areas of distinct folliculitis. On the occiput two lesions, each 3 cm in diameter, showed active follicular inflammation with closely packed crusted papules and pustules. There is generalized dryness of the skin, particularly on the face, where it is tight and erythematous. Keratosis pilaris is generalized.

The results of hematologic examination showed hemoglobin, 85 per cent, erythrocytes, 4,030,000, and leukocytes, 10,900, with a differential count of 68 per cent polymorphonuclears, 4 per cent eosinophils, 3 per cent monocytes, 1 per cent basophils, 22 per cent lymphocytes and 2 per cent large lymphocytes.

Cultures for fungi showed no growth, and there was no fluorescence of the hairs on illumination with the Wood filter

No improvement was noted after the use of pine tar and sulfanilamide ointments

## DISCUSSION

DR G MARSHALL CRAWFORD I suggest the diagnosis of folliculitis decalvans, assuming that favus has been ruled out

DR WALTER F LEVER I should like to add the diagnosis of lichen spinulosus

DR ALFRED HOLLANDER I believe this is a typical case of folliculitis decalvans

DR JOHN G DOWNING As I said to one of the men, I think that if one wants to see a picture of the follicular papules of folliculitis decalvans this is an excellent example of it. In a child of this age, I would not make a diagnosis of pseudopelade or folliculitis decalvans until I ruled out an infectious process. I want to rule out favus or some other type of fungous infection. I think one should go to extremes to exclude pseudopelade, which to my mind is extremely rare

DR EDWARD A LAFRENIERE I suppose that what I am going to say is going to start a great deal of discussion. There is a group of diseases of unknown cause, and they all present distinct clinical pictures but histologically they are almost alike, varying only in the severity of the pathologic process. Now, for instance, pseudopelade shows hardly anything clinically except an atrophy and a slight pink discoloration around the edge, but histologically there is an inflammatory process starting at the neck of the follicle and gradually spreading down to the hair follicle but there is no gross inflammation clinically. Folliculitis decalvans gives a distinct picture clinically and grossly, the inflammatory process is severer microscopically, involving the hair follicle and giving microscopic abscesses. Both will heal with scar tissue and with some sclerosis which is softer in pseudopelade and harder in folliculitis decalvans. There is another disease, perifolliculitis capitis abscedens et suffodiens, which causes an inflammatory process going deeply into the tissue. Then there is the same thing in folliculitis keloidalis, which gives an inflammatory process localized in the follicle with a keloidal ending. I wonder whether twenty years from now these diagnoses will not be changed entirely and based on what is found in the form of an infectious process. For instance, years ago bronchopneumonia and lobar pneumonia, lobular pneumonia and wandering pneumonia were diagnosed as clinical entities, but now a search is made for the type of organism or virus causing the disease. I wonder whether twenty years from now the same thing will not hold true for this group of cutaneous diseases

DR BERNARD APPEL I want to thank all the members for this enlightening discussion. I was much intrigued by Dr Lafreniere's discussion. Dr Lever mentioned lichen spinulosus. I have here a report entitled "Folliculitis Decalvans and Lichen Spinulosus, A Clinical Combination" by Francis Senear published in the Transactions of the Section on Dermatology and Syphilology of the American Medical Association of 1920 in which he says that a number of cases are reported with that well known combination of folliculitis decalvans and lichen spinulosus of the trunk. Although this boy did not show the clinical picture of lichen spinulosus, he nevertheless did have other changes in the skin which are obvious and which fit in with some sort of dyskeratosis that is consistent with the picture previously mentioned that is associated with vitamin A deficiency. Obviously there is some relationship between the hair follicles of the scalp and the follicles of the body. I fear this case is going to turn out to be a case of folliculitis decalvans or pseudopelade or perhaps a superficial case which contains some of the constituents of each of those two pictures

DR FRANCIS M THURMON I believe Senear called attention to the frequent association of lichen spinulosus with folliculitis decalvans and suggested that the toxins elaborated by the disorder of the scalp may be influential in causing lichen spinulosus. In pseudopelade of Brocq there are no pustules. The patient seen today showed pustules

DR JOHN G DOWNING I enjoyed Dr Lafreniere's discussion I do not think one should let it go at that I think he has the right idea One must remember that most of these diagnoses have survived twenty years The reasons that dermatologists go into the intricate diagnosis of these cases are, first, to give the patient a prognosis and to know whether therapy is going to be of any value and, second, as regards therapy, to discover what is going to be used in these cases I think, just looking at these cases, that one should always try to differentiate between this type of folliculitis decalvans, pseudopelade and lupus erythematosus Cultures have to be made, and histologic sections have to be taken

**A Case for Diagnosis (Panniculitis, Nodular, Nonsuppurative?) Presented by DR FRANCIS M THURMON, Boston**

A L., a 68 year old white American woman, has had painful suppurative nodular lesions of the legs for the past thirty-eight years During her youth she was treated for pulmonary tuberculosis, which has been arrested When she was 30, ulcers of the legs were noted, which appeared three months after an immunizing dose of diphtheria antitoxin The onset of each lesion was marked by a pink macule 2 to 4 mm in diameter which was superimposed on a tender nodule 2 mm in diameter The lesion gradually enlarged to form a painful bluish-discolored nodule 2 to 4 cm in diameter which eventually broke down with a serosanguineous discharge Healing was slow, and a depressed atrophic scar resulted The entire clinical course has been afebrile Arthritis deformans has been present

Examination reveals a few varicosities and numerous depressed scars involving the entire surface of the legs, with greatest intensity over the lowest third of the legs The roof of a single lesion is thin and on the verge of erupting, the lesions are dark red, fluctuant and painful Five draining ulcers are present The extremities and fingers are deformed with arthritis

Broth cultures, blood agar plates, agar slants and stained smears failed to reveal organisms Stained smears showed 14 to 200 leukocytes per oil immersion field A guinea pig inoculation was negative for tubercle bacilli The blood sedimentation rate was 41 mm in one hour Examination of the blood showed hemoglobin, 85 per cent, erythrocytes, 4,500,000, and leukocytes, 8,800, with a differential count of 62 per cent polymorphonuclears, 33 per cent lymphocytes and 5 per cent mononuclears

Rapid healing of the lesions followed incision, drainage and irrigation with an 8 per cent solution of glycerite of hydrogen peroxide Iron sulfate, vitamin B complex and ascorbic acid have been administered orally

#### DISCUSSION

DR GEORGE E MORRIS Thirty-five years ago this woman had roentgen rays directed to her thyroid gland as treatment for a "toxic goiter" She knows she had something wrong with her thyroid gland I should like to suggest that she has localized myxedema

DR EDWARD A LAFRENIERE Several years ago Dr Lane and I saw a case of panniculitis The biopsy specimen was not seen by a dermatopathologist The patient had the subcutaneous nodules which developed into sterile abscesses This lady was very thin and emaciated and had an arthritic process in the hands feet and knees, and she appeared to have the picture of tuberculosis I wonder whether panniculitis is not a degenerative process following a toxic disturbance which apparently may be the cause of arthritis and other metabolic disorders

DR LORETTA J CUMMINS In talking with this patient, I was told that when she was a girl she had tuberculosis At least two or three different physicians have diagnosed active tuberculosis of the apexes of the lungs Many of these lesions on the legs have suppurated, and vaccines have been made I do not believe it can be called nonsuppurative panniculitis, with that history

DR C GUY LANE I strongly doubt the diagnosis of nonsuppurative panniculitis in this case. Another curious item to me is the localization in the legs. A group of cases were reported several years ago, and as I remember the lesions involved the thighs and, I am not sure, in one or two instances the calves as well. I think the localization is striking. One wonders whether there is some other factor, perhaps a circulatory factor, perhaps a fat factor, in this particular case.

DR JACOB H SWARTZ I should like to offer a diagnosis of dermatitis nodularis necrotica.

DR FRANCIS M THURMON I thought from the appearance of these lesions that they were infectious but all efforts toward demonstrating this by cultures and smears were unsuccessful. I can conceive of the possibility of a vaccine being made in the past from a contaminant, but I made cultures on blood agar plates, and agar slants and cultures on Sabouraud's medium from three different lesions and they were all sterile. A stained smear of the secretion showed the leukocyte count to vary from 14 to 200 per high power field. There were no organisms, and an acid-fast stain was negative for tubercle bacilli. I could not help but feel that this was in some way associated with tuberculosis in view of the definite history of pulmonary involvement when she was younger. Since that time she has been under the care of good clinicians who assured her there was no evidence of active tuberculosis. A guinea pig was inoculated and the report was negative for tubercle bacilli. There is no history of ingestion of a bromide or an iodide. The character of the lesions rules out erythema nodosum. It seemed to me that the history of the case, with the lesions beginning as small macules 2 to 4 mm in diameter and painful nodes lying beneath the macules going on to suppuration in seven to fourteen days, the lesions occurring in groups and the pain being relieved as soon as the lesions were opened and drained, is suggestive of a liquefying nodular panniculitis of an afebrile type, such as was described by Bailey in 1937. This is not the febrile relapsing nonsuppurative panniculitis because throughout the entire course of the process the patient has been afebrile. As near as I could come to a diagnosis agreeing with the pathologic diagnosis was chronic nonsuppurative panniculitis.

#### A Case for Diagnosis (Psoriasis of the Palms and Soles, Syphilis?)

Presented by DR JOHN G DOWNING, Boston

P Z, an unemployed Polish man aged 42, presents lesions of the palms, soles and anterior surfaces of the arms of approximately eighteen months' duration. In 1937 he presented lesions which were diagnosed as psoriasis, and during the same year was inadequately treated for primary seronegative syphilis. He lapsed treatment until June 1944, when a large calloused indurated pruritic but non-painful lesion appeared on the left heel. Soon the rest of the sole became involved, and similar lesions developed on the right side. Scarring, itching and fissuring of the palms appeared.

Examination reveals thickening, hyperkeratosis and fissuring of the palms and soles, with the periphery sharply outlined by an erythematous induration.

The Hinton reaction of the blood was negative.

Various ointments have been applied and, despite ten treatments with oxophenarsine hydrochloride, potassium iodide orally and low voltage roentgen rays locally, there has been increased intensity in the processes.

#### DISCUSSION

DR WILLIAM P BOARDMAN There certainly have been plenty of psoriatic palms and soles which have not responded to treatment. However, I am wondering whether this is really psoriasis.

DR FRANCIS M THURMON I did not think that the lesions on his elbows and patella were psoriasis. They were follicular and appeared irritated.



DR JOHN G DOWNING When I first saw this man, his hands were in bad shape They were desquamating, infiltrated and hyperkeratotic When he was examined, lesions were found elsewhere He had a past history of syphilis He was given treatment, but the lesions did not respond I should like to know what to do for him

**A Case for Diagnosis (Psoriasis, Lichen Planus, Erythroplasia of Queyrat?)** Presented by DR GEORGE E MORRIS, Boston

C K, a 60 year old white man, has lesions of the glans penis and prepuce which have gradually intensified during the past six months

Examination reveals asymptomatic glistening erythematous infiltrations varying in size from 0.5 to 2 cm in diameter on the glans penis and prepuce A small amount of brown crusting is present

Histologic studies revealed chronic inflammation

DISCUSSION

DR C GUY LANE I do not think that the eruption is erythroplasia This does not have the shine and shape or outline seen in other cases I should feel this was psoriasis in spite of the fact that it is unusually located

DR FRANCIS M THURMON I thought that was typical psoriasis of the genitalia, and did not think it was erythroplasia of Queyrat, because it did not show that shine and glazed surface or the slight thickening that characterizes erythroplasia of Queyrat To be lichen planus of a confluent type such as that particular lesion was, it would have to be a hypertrophic type of lichen planus associated with itching, and itching was not present Clinically, it was typically psoriasis

DR JOSEPH GOODMAN I would agree with Drs Lane and Thurmon about the clinical appearance of this lesion, but the microscopic picture shows infiltrating plasma cells and causes me to believe that it is erythroplasia of Queyrat My conception of erythroplasia of Queyrat is that it is a precancerous dermatitis

DR WALTER F LEVER One may call it that if one wants to preserve the term "precancerous" Erythroplasia, as well as Bowen's disease, was originally described as precancerous, but it seems to me preferable to refer to them as early cancers The characteristic changes are in both diseases, epithelial dysplasia and dyskeratosis, which, I believe, are evidences of early intraepidermal epidermoid carcinoma

DR ALFRED HOLLANDER Clinically this case does not appear to be one of erythroplasia of Queyrat First, there is no shiny appearance, and, second, the lesion is not localized In erythroplasia the lesion would not be so widespread around the penis Histologically this picture is compatible with psoriasis

DR GEORGE E MORRIS Clinically it was psoriasis, but histologically I was not so sure Dr Thurmon and I recently saw a man who was treated for psoriasis of the penis which turned out to be an epithelioma This lesion has some infiltration I think the patient should be watched a little longer

DR JOHN G DOWNING My diagnosis is psoriasis

**A Case for Diagnosis (Dermatitis Medicamentosa?)** Presented by DR JOSEPH GOODMAN, Boston

J A, a 64 year old white man, presents lesions of approximately eight months' duration on the arms and legs

At the onset, lesions appeared on each calf and slowly extended to involve the legs At times these areas were 15 cm in diameter and were minute vesicles, some of which changed to pustules with an erythematous base These spread peripherally, a scalloped border developed, and central healing occurred Vesicles and pustules which recurred within healed areas contained fluid consisting in

great part of necrotic epithelium. Within a few weeks a similar eruption appeared on the arms. Later several areas developed on the forehead and occiput. Over the past two months there has been simultaneous involution of some lesions, while others have appeared. The healed lesions show pigmentation but no scarring. There was no history of ingestion of drugs.

The results of repeated hematologic examinations and urinalyses have been within normal limits. Chemical examination of the blood showed nonprotein nitrogen 42 mg, calcium 9.2 mg and phosphorus 3.8 mg per hundred cubic centimeters. The Hinton reaction of the blood was negative. Two cultures of new lesions yielded no organisms. The histologic examination suggested a drug eruption, particularly of bromide origin.

Local treatment has comprised moist dressings of potassium permanganate, boric acid ointment and low voltage roentgen ray therapy. Sulfadiazine administered in high dosage for two weeks was without benefit.

#### DISCUSSION

DR C. GUY LANE: I saw this case some time ago, and it presents an entirely different picture now than it did at that time. In spite of the patient's denials there is in my opinion a great probability of this being a drug eruption. I do not know whether any reason has been found why he should be taking drugs. Earlier, without the acute phase of the vesicles with the purplish red appearance, there were many more pigmented patches than there are today. There were larger pigmented areas on his arms and less of a mottled appearance. This new acute attack, coming on quickly within a couple of weeks, would emphasize the matter of some toxic or drug factor. I shall be interested to know whether Dr. Goodman has obtained any more of the history.

DR FRANCIS M. THURMON: I happened to stand behind the curtain when this patient was talking to somebody else, and he seemed to me to be somewhat of a verbal exhibitionist and glad to show himself off and talk about his dermatitis. I would not be surprised if this proved to be a factitious condition precipitated by the ingestion of phenobarbital or phenolphthalein.

DR LEONARD E. ANDERSON: I am in accord with Dr. Thurmon and should like to see how he gets along on fixed dressings for a while.

DR G. MARSHALL CRAWFORD: Another possible factor is that the patient knows he will not be operated on for his hernia as long as he has this eruption.

DR JOSEPH GOODMAN: I have questioned this patient repeatedly about ingestion of drugs, before and after he saw Dr. Lane. On no occasion could I uncover anything that was suspicious. He runs a tavern and works behind the bar, and says that he has taken an occasional drink of rye but no mixed drinks, no cocktails and no wines. I have been unable to reach any conclusion other than that he has an eruption caused by a drug, but I am unable to find any history to support it. As to his tendency toward exhibitionism, I have been attempting to get him to a meeting for six months. It was with reluctance that he came today. He does not seem inclined to want to show these lesions to any one.

#### A Case for Diagnosis (Sarcoid, Leprosy, Lupus Erythematosus?)

Presented by MAJOR EARL A. GLICKLICH, Lovell General Hospital, Fort Devens, Mass.

V. B., a 26 year old white man, a commissioned officer in the Army, presents lesions of the face and left hand of eight months' duration. He had been in the service for four years, twenty-one months of which had been spent overseas in Hawaii. He first noticed circular erythematous lesions on the right malar region in June 1944. He received six treatments with bismuth subsalicylate, stomatitis developed, and the use of bismuth was discontinued. He then received eight doses of gold sodium thiosulfate totaling 210 mg, with decided improvement. He left on detached service for five weeks, and on his return the original areas

recurred and grew larger. He stated that the area was practically anesthetic. In addition he gave a history of a similar lesion occurring on the knuckle of the left index finger, of two years' duration, and of a lesion that developed more recently on the left ring finger.

With the exception of the cutaneous involvement, the physical findings are within normal limits. There is an oval indurated macular erythematous patch of dermatitis in the right malar area which is scaling and shows follicular dilatation. No telangiectasis is present. Similar lesions, although less extensive, are present on the knuckle of the index finger of the right hand and the third finger of the left hand.

The results of the examinations of the blood and the urine, as well as those of roentgenographic examinations of the chest, hands and feet, were within normal limits. Histologic examination showed essentially a tuberculoid structure.

#### DISCUSSION

DR E. MYLES STANDISH: I thought the diagnosis was sarcoid. That seemed to fit well the lesions as shown and also the biopsy.

DR BERNARD APPEL: I felt clinically it was sarcoid, but as the question of leprosy had been raised I wonder why an intradermal injection of histamine phosphate has not been given. This is a definite test which was well described by Pardo-Castello and is almost specific for macular forms of leprosy.

MAJOR EARL A. GLICKLICH: How shall this man be treated? He has already had a bismuth preparation.

DR ALFRED HOLLANDER: I propose the use of chaulmoogra oil. You will remember that several months ago Dr Cheever presented the case of a young boy who had a similar lesion on the forehead. I recommended to Dr Cheever the use of chaulmoogra oil and he told me later that the lesion had improved. I have had good results with injections of chaulmoogra oil in some cases of sarcoid.

DR JOHN G. DOWNING: I suggest injections of diphtheria toxoid.

DR FRANCESCO RONCHESE: If it is sarcoid, it may spontaneously disappear.

DR ALFRED HOLLANDER: Regarding the diagnosis of leprosy, I believe leprosy lesions will not appear in such a short time. A lesion of leprosy will not appear before five or six years after exposure.

#### A Case for Diagnosis (*Sycosis Vulgaris* and *Folliculitis* of the Scalp?)

Presented by DR BERNARD APPEL, Lynn, Mass.

J. K., a 23 year old white man, presents lesions of the face, scalp and pubis of two years' duration.

Two years ago, while he was employed as a welder in the Navy Yard, minute pustules developed on the bearded area of the face and on the back of the neck at the hair line. The lesions were moist, but the inflammation was minimal. At this time treatment with *Staphylococcus* vaccine, ultraviolet rays and roentgen rays produced improvement. He then was inducted into the armed services, and while he was stationed in Texas an exacerbation of these lesions occurred, with additional involvement of the scalp. Penicillin and local therapy produced no improvement. He then received a medical discharge.

Examination reveals involvement of the bearded areas with numerous small yellowish pustules on an erythematous raised indurated base. Hairs penetrate many of these discrete papules. The pubic area is similarly involved. On the scalp there are nontender red nodular perifollicular infiltrations. Numerous areas of alopecia with minimal scarring are present on the vertex.

The results of the urinalysis were normal. The blood count showed hemoglobin, 102 per cent (Sahli), and leukocytes, 7,200 with a differential count of

60 per cent polymorphonuclears, 36 per cent lymphocytes and 4 per cent mononuclears. The results of cultures have not yet been reported.

## DISCUSSION

DR EDWARD A. LAFRENIERE: This is a case which seems to emphasize the point which I tried to bring out a little while ago. This man's disease started with sycosis of the beard, which spread to the scalp, giving him folliculitis. Three days ago there was a small area of furfuraceous scaling on the chin which I suspect was a fungous infection, probably complicated with a secondary staphylococcal infection. I understand that in cases of sycosis vulgaris it is not common for scar tissue to develop, although it does happen, as it did in this case, spreading to the scalp and giving some areas of thin, atrophic skin, some areas of a nodular type of lesion and several areas which are almost abscessed. Then the patient has lesions on the face which are suggestive of the papules of acne, some are secondarily infected—all of which leads to the conclusion that most human beings inherit a certain type of skin which may have allergy or anergy and may be susceptible to certain types of infections. This in addition to a staphylococcal infection, as in this case—a different strain of *Staphylococcus*—will give a different type of manifestation—a different type of location and different types of end lesions.

DR FRANCIS M. THURMON: I believe, since it is known how persistent this entity is, one would not be justified in giving him a five day course of penicillin therapy.

DR CARL D. SAWYER: Long ago I had a patient with extensive sycosis vulgaris, and I gave him a course of fractional doses of roentgen rays which cleared it, but after three or four weeks it broke out again.

DR GEORGE E. MORRIS: I have a similar patient who has been seen by several physicians. He has had twenty-five roentgen ray treatments. He has had a good course of treatment with penicillin and sulfonamide compounds. He heard somebody recommend sulfur ointment. He got it from a druggist, and within two weeks he was better than he had been with all the ointments that had been prescribed for him.

**Lupus Vulgaris** Presented by DR. FRANCESCO RONCHESE, Providence, R. I.

J. S., a 28 year old white man, an American-Italian farm worker, presents a lesion of approximately eleven years' duration on the right side of the head and face. At the time he was first seen, in 1935, he presented a yellowish red nodular lesion on the right temple (See figure). This lesion was destroyed by desiccation and curettage, resulting in an apparently well healed scar. However, one year later new lesions appeared at the edge of this scar and have continued to extend peripherally.

The active lesions are scaling raised soft nodular areas, involving the right side of the forehead, eye and cheek, and recently the conjunctiva of the right eye has been affected. The central portion of the area shows scarring and atrophy, resulting in part at least from therapy.

The Hinton and Wassermann reactions of the blood have been negative repeatedly. The reaction to tuberculin was positive. A histologic examination confirmed the diagnosis of lupus vulgaris.

Treatment has comprised desiccation curettage, plastic surgery, use of roentgen rays, radium and radon implants, application of an ointment containing pyrogallol in a concentration of 10 per cent, bismuth therapy, injection of oxophenarsine hydrochloride, a salt-free diet and injection of Eulykol (phenylethyl esters of a selected fraction of the acids of hydnocarpus oil prepared by Burroughs Wellcome & Co. Inc.) and starch. (Starch is recommended as beneficial in lupus vulgaris.)

A saturated solution of corn starch in sterile saline solution is used ) An area on the right eyebrow was excised and grafted The process has now involved the grafted area, together with the skin and the mucous membrane of the right eyelid



Lesions of lupus vulgaris A, in 1935, B, in 1939, C, in 1944

#### DISCUSSION

DR LEONARD E ANDERSON His pictures show that nothing has been accomplished so far The small lesion which developed in 1935 has become

extensive, and I think his only salvation is to find somebody bold enough to excise it

DR ALFRED HOLLANDER I believe this is a typical case of lupus tumidus. In such cases the lesions have a tendency to develop into real keloids. I should be careful in going far into it because one may get rid of the lupus and new keloids will develop. I propose the Gerson-Hermannsdorfer diet for a therapeutic trial.

DR FRANCIS M THURMON I think that no matter what is done for this man he will get worse.

DR FRANCESCO RONCHESE This case followed for eleven years offers a good example of what one may expect from treating an early lesion of lupus vulgaris otherwise than by wide surgical excision especially when the area, as in this case, is well suited for such a procedure.

This case was presented before the New England Dermatological Society on April 12, 1939 (Lupus Vulgaris [Tumidus], *ARCH DERMAT & SYPH* 41 427 [Feb.] 1940). As the "tumidus" variety of lupus vulgaris does, its clinical appearance resembled a nevus. Its unusual features are demonstrated by the discussion which followed. Its pathologic picture was that of tuberculosis of the skin, with acid-fast bacilli and with inoculation of the guinea pig being followed by development of tuberculosis. This patient has been followed since 1935, when the original lesion on his right temple (shown in the figure) was desiccated and curetted, resulting in a good scar and an apparent cure. The patient did not return as he was advised to do for observation. When he was seen again, six months later, a crop of new lesions had developed around the edges of the scar. The eruption has peripherally advanced ever since.

Surface application of radium, radon implantation and roentgen irradiation gave the best result, as clearing can be seen in the central area. However, these procedures failed to stop the peripheral advance. The injections of Eulykol and starch and the antisyphilitic therapy and the application of 10 per cent pyrogallol ointment had no effect whatsoever. A salt-free diet was prescribed, but as usual it cannot be followed properly if the patient is not hospitalized. An area on the right eyebrow was successfully excised and a graft applied. At present the disease has involved the grafted area and the skin and the mucous membrane of the right eyelid.

DR FRANCIS M THURMON I saw a patient with lupus worse than this at the Atlantic Dermatological Conference in Washington ten years ago. His condition was a good example of what this disease will finally become.

NOTE—From January 1946 to August 28 the patient received calcium gluconate, 10 cc, intragluteally, three times a week and 25 mg of crystalline vitamin D<sub>2</sub> (Drisdol, Winthrop Chemical Company, Inc.), daily, by mouth, according to the method suggested by Charpy (*Bull Soc franç de dermat et syph*, November-December, 1943, p 340). No ill effect from the medication has been noticed. The calcium content of the blood varied from 10 to 10.5 mg per hundred cubic centimeters. The result has been most gratifying. The tumid lesions have flattened down completely to brown hyperpigmented areas. No new peripheral lesions have appeared. There is no more discomfort. The lesions appear to be healing completely.

In the last few months other patients having lupus vulgaris were treated in the same way, with encouraging results.

## CHICAGO DERMATOLOGICAL SOCIETY

Frederick R. Schmidt, M.D., *President*Marcus R. Caro, M.D., *Secretary*

Feb 21, 1945

**A Case for Diagnosis (Cutaneous Leishmaniasis?)** Presented by DR E M SMITH JR

T. T., a white woman aged 43, complains of multiple chronic ulcers of the skin. While in Florida in March 1937 she noticed a tiny hole in the skin, with a slight discharge. Several more of these sinuses appeared but never with an acute inflammatory reaction. In June her physician cauterized the area with actual cautery, but the discharging sinus persisted and a new one appeared 2 inches (5 cm) from the original one. Repeated attempts at excision of the area have resulted only in a spread of the process. The patient was seen in the clinic of St. Luke's Hospital in February 1938, at which time she had several large ulcers on the back, which did not seem deep and had little inflammatory reaction around them. The skin was undermined for a distance of about half an inch (1 cm). Various dressings made little improvement. The ulcerated lesions on the back healed after thirty-six injections of stibophen (Fuadin), the last injection being given in April 1939. In August 1944 the patient returned with a similar ulcer over the area of the right biceps muscle. This lesion had been present for five years. During the interval she had been without treatment and without improvement, according to her statement.

An intramuscular injection of a small dose of the antimony preparation resulted in collapse of the patient. In October 1944 she noticed a tender nodule appearing in the subcutaneous tissues over the area of the left deltoid muscle. This lesion had a tendency to come to the surface and has been removed for histologic examination. At the present time there is another nodule in the same area.

Two inoculations of a guinea pig with material from the ulcer produced no pathologic changes. A roentgenogram of the chest showed no recent pathologic changes, "there is some old thickening in both lower lobes especially the right, with probably some bronchiectasis." A recent smear showed no acid-fast bacilli. Gram stains showed many leukocytes and erythrocytes but no organisms. Aerobic and anaerobic cultures showed no growth in seventy-two hours. Sodium hydroxide preparation showed no fungi or mycelial threads. No actinomycetes were found on the dextrose agar plate, but one culture showed a light count of *Staphylococcus aureus*. The dark field illumination did not reveal any trypanosomes or similar organisms. The Kahn and Wassermann tests were consistently negative.

A histologic section removed from the subcutaneous nodule showed non-circumscribed areas of focal necrosis deep in the stratum corneum and extending into the fat layers, such as might suggest embolic foci of necrosis, and chronic granulation of subcutaneous fat tissue such as might be found in a case of embolic tuberculosis. No *Leishmania* bodies were identified.

## DISCUSSION

There was no discussion of this case.

**Iododerma with Secondary Streptococcal Infection** Presented by DR FRANCIS E. SENEAR, DR MARCUS R. CARO and (by invitation) DR C. H. STUBENRAUCH JR

F. H., a white woman aged 36, was seen for the first time at the University of Illinois in December 1944, at which time she presented a palm-sized ulcerated, vegetating and scarred area on the extensor surface of the left forearm. This lesion had been present for eight months. During this time it had become worse on two occasions, after the administration of sulfonamide compounds and after the

start of a course of injections of sodium iodide. One week before this first visit several new abscesses had appeared on the left forearm and the right leg. The patient had been taking a tonic containing potassium iodide for several days previous to the development of these new lesions. She stated that she had taken no medicament previous to the onset of the original lesion but admitted using iodized salt freely.

At the time of the patient's first visit to the clinic a pure culture of hemolytic streptococcus was obtained from each of several unruptured abscesses. The patient was given 1,200,000 units of penicillin intramuscularly in the course of about two weeks, with resultant healing of all abscesses and improvement in the vegetating lesions on the left forearm and the right leg.

The patient returned to the outpatient department yesterday and stated that the present lesions had become active when she received sulfathiazole after a miscarriage a few days ago.

The histologic examination of a section removed from the lesion of the forearm showed suppuration and the presence of many cocci.

#### DISCUSSION

DR FRANCIS E. SENEAR. The interesting thing in this case, in addition to the findings which were presented and also brought up in the history, was that the patient had a dermatitis as a result of her ingestion of one of the sulfonamide compounds while in the hospital for treatment of this iododerma complicated with streptococcal infection. She made a complete recovery and was discharged. Then some one gave her one of the sulfonamide compounds, and she had a recurrence in the original site of the iododerma. I have seen 1 or 2 instances in which there was a focal reaction following ingestion of a sulfonamide compound in a patient who had a dermatitis due to some other agent. I wonder if any one else has made any observations in similar cases.

#### A Case for Diagnosis (Purpura Annularis Telangiectodes?) Presented by DR FRANCIS E. SENEAR and DR MARCUS R. CARO

F. A. J., a white woman aged 53, first noticed a small red patch above the right cubital fossa about two and a half years ago. When she first came under our observation, on Aug. 8, 1944, there were several lesions on the flexor surface about the right elbow. Several other lesions have appeared since then, and these have gradually increased in size.

At the present time there are several poorly outlined patches, from the size of a pea to that of a dime, above and below the right cubital fossa. They are slightly erythematous, the erythema being almost entirely expressible. There is slight atrophy in the lesions, and small purpuric macules and telangiectases are present. There are no symptoms.

The urine was normal. The Wassermann and Kahn tests of the blood were negative. An examination of the blood showed 4,200,000 erythrocytes and 8,600 leukocytes, with a differential count of 44 per cent lymphocytes and 56 per cent neutrophils. The hemoglobin content was 85 per cent.

A histologic section taken from a lesion showed the epidermis to be flattened, with intracellular edema of the basal layer. Some of the superficial blood vessels were greatly dilated, while others were surrounded by circumscribed mantles of densely packed infiltrating cells, largely lymphocytes. Weigert's stain showed the elastic fibers to be destroyed in the areas of infiltration.

#### DISCUSSION

DR L. H. WINTER, Minneapolis. The microscopic section shows much more than one would be led to think was present from the clinical picture. Cells of many types participate in the infiltration but the preponderant cells appear to be those that tend to form capillaries. There are also dilated capillaries in the section.



This infiltration is rather extensive, and, as a result of the microscopic appearance, I should favor a diagnosis of angioma serpiginosum of Hutchinson

DR M J REUTER, Milwaukee I was nonplussed when I observed the patient I did not see the histologic section I considered the diagnosis mentioned by Dr Winer (angioma serpiginosum of Hutchinson), but I thought that the diagnosis was probably purpura annularis telangiectodes because I believed that there was definite purpura present

DR MARCUS R CARO When the patient first came in to see us, the lesions were so insignificant that I wondered why she bothered about them They seemed to be patches of slight dermatitis that should have responded to simple medication like the application of zinc oxide ointment In spite of treatment, however, they continued to enlarge, and biopsy was performed We were surprised to see the amount of pathologic change, which was greatly out of proportion to the clinical appearance I do not believe that the pathologic observations fit in with the diagnosis of purpura annularis telangiectodes or angioma serpiginosum, but I cannot make a definite diagnosis

**Parapsoriasis Guttata (Pityriasis Lichenoides Chronica)** Presented by  
DR STEPHEN ROTHMAN and DR H KRYSA (by invitation)

A S, a white girl aged 16, was first seen in the University of Chicago clinics on Jan 19, 1945 She presented a widespread papulosquamous eruption of ten to twelve days' duration, which was slightly pruritic She gave a history of getting a vesicular eruption whenever she took cod liver oil or goose fat She also had had "psoriatic spots" at the age of 6 or 7 years Four years ago she was ordered to take thyroid because of obesity, and since that time she has been taking this drug with short interruptions The basal metabolic rate has varied from —16 to —20 per cent When she was first seen, she was taking iron, calcium and vitamins in irregular doses at irregular intervals Twelve days prior to the appearance of the eruption, the patient had a sore throat and took sulfathiazole, 4 Gm the first day and less on the second day Ten days later the eruption appeared, first on the front of the neck and on the hands and the arms, and then spread rapidly to become generalized

The eruption consists of discrete, sharply circumscribed, scaling erythematous lesions, 2 and 3 mm in diameter The scale on some lesions can be removed like a collodion membrane There is no bleeding phenomenon

The urine was entirely normal The Kahn test was negative The blood showed hemoglobin, 14.3 Gm, erythrocytes, 4,360,000, leukocytes, 7,700, with a differential count of 62 per cent neutrophils, 26 per cent lymphocytes, 9 per cent monocytes and 3 per cent eosinophils The basal metabolic rate was +12 per cent A fluoroscopic examination of the chest showed no pathologic changes

A histologic section taken from a lesion showed parakeratotic scales and a chronic inflammatory perivascular papillary and subpapillary infiltrate

Ultraviolet irradiations and applications of ammoniated mercury ointments have been ineffective up to the present time

#### DISCUSSION

DR H E MICHELSON, Minneapolis Often I see a patient for whom the diagnosis rests between psoriasis and parapsoriasis, and usually when there is much question I find that eventually the disease turns out to be psoriasis In this particular case there is not much in the microscopic picture that points to psoriasis

DR MAURICE OPPENHEIM (by invitation) The differential diagnosis between psoriasis and pityriasis lichenoides chronica is difficult in the case presented today The form of scaling speaks more for psoriasis despite the absence of bleeding The color and the location are more common in psoriasis I did not see the histologic section, but I think that the disease is a superficial form of psoriasis

DR S W BECKER The histologic section is not typical for psoriasis, but the mother stated that the child had had a psoriasis-like eruption at the age of 6 or 7 years. It would seem to be in favor of a diagnosis of psoriasis rather than parapsoriasis because the eruption disappeared entirely and recurred only recently.

DR FREDRICK R SCHMIDT Simply stroking the skin will produce redness due to increased vasolability. It is present in most cases of parapsoriasis. That phenomenon is absent in this case.

DR FRANCIS E SENEAR I should like to add one more piece of evidence in favor of psoriasis. I scraped a good many of those lesions but could not find anything except a minimal amount of scaling, not the powder-like scaling seen in parapsoriasis after guttage.

**A Case for Diagnosis (Fat Necrosis?)** Presented by DR L F WEBER and DR IRENE NEUHAUSER

F W, a woman aged 38, four months ago had an acute exacerbation of undulant fever following an infection of the upper part of the respiratory tract. The cutaneous and agglutination tests revealed the presence of undulant fever at that time. Since Nov 6, 1944 the patient has received twenty injections of undulant fever vaccine at the rate of two a week. The vaccines of both Parke, Davis & Company and Lederle Laboratories, Inc., were used. A severe systemic reaction accompanied each injection. Severe local reactions also occurred, not only in the area in which the vaccine was given but at the sites of previous injections. The site of the original cutaneous test, which was indurated and inflamed, would also flare up and drain.

Examination reveals many superficial and deep firm nodules varying in size from that of a pea to that of a hickory nut on the extensor surfaces of both arms. On the extensor surface of the right arm and on the left thigh are bean-sized fluctuating areas. On the right thigh there is a similar lesion, which is draining. On the flexor surface of the left forearm is an erythematous, indurated, scarred area, which is practically crust covered.

A nodule over the region of the right triceps muscle was removed for histologic study, and the surgeon reported that macroscopically it appeared to be an area of fat necrosis surrounded by a cyst wall. This material when cultured yielded no organisms. The fluctuating area in the same region was aspirated several times and a clear fluid obtained, which appeared to be a liquid fat.

The histologic examination of a section from the nodule showed that it consisted of an inflammatory cyst, the cyst wall was composed of a chronic granuloma with considerable fibrosis. Many of the cells were foam cells, but staining for lipid substances could not be done because the specimen had been prepared in alcohol.

DISCUSSION

DR MARCUS R CARO About ten years ago Dr Wien and I reported 3 cases of traumatic epithelial cysts of the skin (*Traumatic Epithelial Cysts of the Skin, J A M A* 102:197 [Jan 20] 1934). In 2, the lining membrane was composed of epidermis, while in the third case it was a layer of chronic granuloma and fibrosis similar to that seen in the present case. Unfortunately the fat stain could not be obtained in this specimen, but a number of foam cells were present, suggesting that fat was present. About a year ago Dr Cornbleet presented before this society a girl with a number of ulcers on the skin at the site of injection of protamine zinc insulin. Histologically these also showed cystic granuloma formation. In the present case one may be dealing with fat necrosis or a foreign body reaction.

DR PAUL O'LEARY, Rochester, Minn Lesions of this type are occasionally seen following injections of insulin, pituitrin and an extract of adrenal cortex. I do not believe that a toxic product in the preparation is the cause of the necrosis because I have observed 2 patients who received injections from the same ampule,

1 of whom had a large nodule which became necrotic while the other patient had none. The former patient had been having similar reactions from previous injections. I have accordingly been impressed with the possibility that reactions of the type displayed by the patient presented are the result of an immunologic or an allergic state of the patient rather than the result of administration of an impure product.

DR IRENE NEUHAUSER. Apparently this type of reaction is not uncommon with undulant fever. Usually this reaction does not occur with the abortus strain but does occur with the melitensis and suis strains of *Brucella*. Since investigators have found that the abortus strain is just as effective when used therapeutically, it might be better to use this strain.

**Acanthosis Nigricans Juvenilis?** Presented by DR I M FELSHER and DR E P LIEBERTHAL

C K, a white girl aged 15, was admitted to the dermatologic department of the Mandel Clinic of Michael Reese Hospital on Dec 5, 1944. At that time she presented subcutaneous lesions in the supraclavicular areas, on the sides of the neck and in the axillas, characterized by dark brown pigmentation and numerous soft, reddish brown papules or verrucous growths, varying from 1 to 3 mm in diameter and of more than two years' duration. The pigmentation was lighter at the periphery of these areas. There was no complaint of any subjective symptoms. The patient was somewhat retarded mentally. Her father had active pulmonary tuberculosis about ten years ago. The disease is now in an arrested state.

At the present time the results of a physical examination and laboratory studies including a complete blood count, a urinalysis, a chemical examination of the blood, an examination of the stool, a determination of the basal metabolic rate and a study of roentgenograms of the chest, are all within normal limits. Serologic tests for syphilis gave negative results.

A histologic section taken from a lesion of the left supraclavicular area revealed acanthosis, hyperkeratosis and hypertrophy of the granular layers in parts, with a definite increase of pigment in the lower rows of the rete and the basal layer. There were also numerous chromatophores loaded with pigment in the papillae and the subpapillary layer of the corium. The blood vessels were surrounded by a chronic inflammatory infiltrate and chromatophores that had some granular pigment.

#### DISCUSSION

DR CLARK W FINNERUD. I did not see the sections, but I thought that the eruption was Darier's disease, judging from the lesions of the neck, but the lesions of the lateral surface of the arms I thought were keratosis pilaris. I think that this would be an excellent case, from the standpoint of both of these disorders, in which to try out on intensive therapy with vitamin A.

DR CARL W LAYMON, Minneapolis. I agree with Dr Finnerud that the case is one of keratosis follicularis. The lesions on the hard palate are consistent with such a diagnosis.

DR LOUIS A BRUNSTING, Rochester, Minn. I agree with Dr Finnerud. The girl is said to have mental retardation as well.

DR PAUL O'LEARY, Rochester, Minn. This patient presented another feature of Darier's disease, namely, the tendency to become moderately improved or to become greatly improved during the winter, only to have the keratotic lesions recur during the summer months.

DR I M FELSHER. When we first saw the patient in December, the picture presented was entirely different from what it is today. The patient had diffuse pigmentation that was dark, in those areas, and verrucous lesions about five or six times the present size. We considered immediately the possibility of Darier's disease. However, I labeled this presentation "acanthosis" for the sole purpose of provoking a discussion, particularly on the possibility of obtaining beneficial

effects with vitamin A in instances of acanthosis nigricans juvenilis. This patient has received 100,000 units of vitamin A daily in the last three months, and she has made noteworthy improvement. At present there is little pigmentation left, and the verrucous lesions have cleared to about one fifth of their former size. The histologic section showed sufficient dyskeratosis to be compatible with keratosis follicularis, but the hyperkeratosis and increased pigmentation could also include the possibility of acanthosis nigricans juvenilis.

**Epidermolysis Bullosa (Acquisita)** Presented by DR EDWARD A OLIVER  
and (by invitation) DR A GREENBERG

B R., a man aged 32, suffered repeated attacks of a bullous type of eruption on the hands, brought on by any type of trauma, of two years' duration. These lesions ruptured and occasionally became infected. The same process occurred on his neck, probably due to collar irritation. No other areas have been involved. The patient has undertaken careful family research but has found no similar or related disease.

A physical examination two weeks ago showed some small bullous eruptions on the dorsal outer aspect of both hands. These lesions contained a clear, watery serum which was sterile on culture.

DISCUSSION

DR LOUIS A BRUNSTING, Rochester, Minn. In the acquired type of epidermolysis bullosa, especially when bullous lesions appear on the exposed surfaces of the skin, it may be well to look for a possible disturbance of porphyrin metabolism. Sometimes there are melanosis and hypertrichosis as well and also vague abdominal symptoms and an indeterminate decline in general health, particularly an unexplained loss of weight. In one such patient in my experience recently, a woman in her fifties, such a train of symptoms was explained on this basis. There were large amounts of uroporphyrin in the darkened urine and also some indication of impaired hepatic function. With regard to my patient's sister, porphyrinogens were demonstrated in the urine, although she was in perfect health. This indicates that such a disturbance of metabolism may be familial and perhaps may remain dormant throughout life.

**Generalized Erythroderma with Lipomelanotic Reticulosis (Pautrier and Worringer)** Presented by DR EDWARD A OLIVER and (by invitation)  
DR A GREENBERG

J L., a Negro man aged 33, contracted bilateral inguinal adenopathy while he was stationed in the southern part of England in January 1943. This was followed by spreading, extensive scaling and pruritus of the skin. There is no family history of ichthyosis or memory of a previous similar episode in childhood.

Physical examination reveals scaly lichenification of the upper extremities, the hands, the abdomen and the lower extremities. There is generalized adenopathy, with the inguinal region being most involved.

The serologic study showed no evidence of syphilis, and the blood counts were within normal limits.

A histologic section from one of the lesions is presented.

DISCUSSION

DR S W BECKER. I think that when a severe dermatitis develops in a patient he does a lot of scratching, and the glandular enlargement in this case may be due chiefly to secondary infection. Evidently considerable pigment is absorbed from the deeply pigmented epidermis and is deposited in the lymph nodes. I think that this patient has pronounced lymphadenopathy, with melanosis of the lymph nodes secondarily.

DR RUBEN NOMLAND, Iowa City. After reading the original article on this disease I became interested and made several histologic sections of lymph nodes of

patients who had generalized exfoliating dermatitis and enlargement of the lymph nodes. Both lipid substances and pigment were present in the lymph nodes, but the general pathologists did not think this unusual. They said that melanin pigment and probably lipid material are found at most autopsies in which they examine the lymph nodes. They thought that it was nothing but a phagocytosis of foreign material derived from the skin and elsewhere. It is probably more pronounced in exfoliative dermatitis because of the inflammatory condition of the skin.

#### **Mycosis Fungoides** Presented by DR OLIVER S ORMSBY

R E, a man, has had the present disorder for five and a half years. The eruption began on the right flank and gradually spread over the entire body. When the patient was first seen by me two and a half years ago, there was a diffuse eruption involving the neck, the trunk, the front, the arms, the forearms, the thighs and the legs. The lesions consisted of crescentic, round and oval plaques, moderately elevated and varying in size from that of a small coin to that of a palm. Numerous plaques had depressed centers and elevated margins.

The patient has had roentgen ray therapy almost constantly for three years. A large number of the plaques have cleared, but new ones have developed. The eruption has been associated with much itching. Asiatic pills (a preparation of arsenic trioxide and black pepper) given for the last three years together with the roentgen ray therapy have kept the disease under control.

About three years ago a histologic study of a section taken from one of the lesions confirmed the clinical diagnosis of mycosis fungoides.

#### DISCUSSION

DR PAUL O'LEARY, Rochester, Minn. I believe that chaulmoogra oil and fever therapy make the patient with mycosis fungoides more comfortable and occasionally slow up the progress of the disease. Perhaps this observation is due to the fact that the patients treated in this manner had a mild form of the disease and were destined for a long, protracted course. Nevertheless, the pruritus has been definitely decreased. A number of patients thus treated eventually presented exfoliative reactions and bizarre features of the disease that clinically were not typical of mycosis fungoides. In several cases in which roentgen ray therapy had been given to the point where the plaques did not melt out after its further use and after a course of chaulmoogra oil and hyperthermy, the plaques faded out after further treatment with roentgen rays.

DR OLIVER S ORMSBY. I presented this patient on account of the fact that he has had this disease for five and a half years. It has been extensive. It was treated with roentgen rays locally and with arsenic internally. I think that this treatment has held the disease in abeyance. A patient who has been so severely affected as this patient has been would usually have had serious results in five and a half years.

#### **Calcinosis in a Burn Scar** Presented by DR EARLE R. PACE.

J O, a man aged 37, suffered a severe burn of the right pectoral region at the age of 7 years. The resulting scar was soft and supple except for an irregular firm area at about the site of the missing right nipple. About six or eight months ago this keloidal tissue was torn open while the patient was lifting heavy crates. A physician prescribed a cod liver oil ointment, which has been used continuously since that time.

When seen two weeks ago this patient presented a roughly triangular granulomatous lesion with a rolled, friable border, which was elevated about 3 mm. This was continuous around what appeared to be a central hard black blood "crust." Attempts to remove the "crust" led to profuse bleeding. The initial impression was that of an epithelioma with a peculiarly tough blood crust. Histologic examination of a section taken from the upper rolled border showed granulation tissue, with no evidence of malignancy.

Subsequent efforts to remove the "crust" revealed it to be bony-hard and evidently calcareous. Chunks were cut away with a heavy bone snip. After the decalcifying procedure these fragments showed no cellular structure.

In addition to this spike, which originally measured about 25 by 10 mm, there are two small circular deposits above the principal lesion which have bared their surface during the past two weeks. Much of the large spike has been cut away. Roentgenograms suggested that the calcinosis was relatively superficial. There is now present a palpable subcutaneous hard cord extending upward about 4 cm from the ulcer. Surgical excision of the area and grafting are contemplated, and suggestions are invited.

The histologic section from the ulcerated area showed the histologic changes of a chronic granuloma containing considerable iron pigment. The other specimens were completely calcified.

#### DISCUSSION

DR EARLE R. PACE: There was much more to the picture about two weeks ago. It was a granulomatous mass with a huge blood clot in the center. At the time I took the histologic section it was friable. I do not know whether the members palpated the lesion, but there was a core of calcium in the center plus extensions upward under the skin. I would be interested to know if any one has an idea of how to get rid of that core.

#### Symmetric Melanosis (of Genetic Origin?) Presented by DR STEPHEN ROTHMAN and DR H. KRISA (by invitation)

R. P., a Negro man aged 37, had been in perfectly good health and had never had any disease of the skin until 1930 when he noticed freckle-like spots on both cheeks, which grew until they occupied almost the entirety of both cheeks. In the past five or six years his eyebrows have become thinner, and patches of hyperpigmentation have appeared on the skin of the supraorbital ridges. Recently he noticed similar spots in front of his ears. No itching or reddening preceded the appearance of these spots. An aunt who died many years ago was said to have had a similar hyperpigmentation.

Physical examination reveals strictly symmetric patches of hyperpigmentation of a dark brown shade on both cheeks. The skin is smooth, oily and apparently of normal texture and contains a normal amount of hair follicles. There are also two symmetric horizontal patches parallel to, above and below, the outer seven eighths of both eyebrows. The left of these meets the left patch of the cheek. The outer parts of the eyebrows are sparse and short.

Histologic sections taken from the preauricular area showed an atrophic epidermis and dilated follicular pores but no signs of lupus erythematosus. Histologic sections treated according to Becker's dopa method showed moderate dopa activity. Silver stain showed hyperpigmentation.

#### DISCUSSION

DR S. W. BECKER: I talked to this man briefly, and I think that he has typical chloasma, which is not uncommon. I do not know how frequently it occurs in families. Both histologically and clinically it is chloasma.

DR MAURICE OPPENHEIM (by invitation): The disease reminds me of melanosis caused by essential oils like oil of bergamot, by lubricants and by tar products.

DR S. W. BECKER: The histologic sections showed that the melanosis was limited to the epidermis, which is different from the picture shown in melanosis due to sensitization. In the latter condition there is a lot of melanin in the chromatophores, and the color is grayer.

**Subacute Disseminated Lupus Erythematosus** Presented by DR STEPHEN ROTHMAN and DR H KRYSA (by invitation)

S K, a woman aged 36, was first seen in the University of Chicago clinics on Sept 29, 1944. She presented the typical picture of chronic discoid lupus erythematosus, with lesions on the scalp and both ears and above the right upper lip. The patient stated that she first noticed patches of alopecia of the scalp five years ago and that since that time these have spread steadily and progressively. Otherwise the personal and the family history were noncontributory.

The urine was normal. The serologic tests were negative. The blood count showed 5,000 leukocytes, 3,950,000 erythrocytes and a hemoglobin content of 12.4 Gm. Chemical examination of the blood revealed nonprotein nitrogen 19 mg and total serum protein 7.7 mg per hundred cubic centimeters and an albumin-globulin ratio of 4.89:2.81, equaling 1.74.

Histologic sectioning of the cutaneous lesions was not permitted.

The patient was given a course of weekly intravenous injections of ammonium succinimidoaurate. She received 25 mg on September 29, 50 mg on October 5, 75 mg on November 1 and 100 mg on November 10. The leukocyte count and the urine were checked during this course several times and were found to be normal. On November 15, five days after the last injection, the patient presented herself with an erythematous and papular eruption occurring on the dorsa of the hands, the palms, the forearms and the soles in the fashion of a toxic eruption. There was intense itching but no systemic sign or symptom, particularly, there was no stomatitis, enteritis or renal damage. The leukocyte count was 5,600. Sodium thiosulfate was ordered, to be taken intravenously and orally.

Since November 1944 the eruption has slowly improved, but it is still persisting. It now consists of reddish to violaceous macules, some of them displaying adherent scales, partly diffused over the macule, partly held in follicular plugs. The patient has again refused to have histologic sections taken.

## DISCUSSION

DR LOUIS A. BRUNSTING, Rochester, Minn. The patient presents discoid lupus erythematosus of the face, and the widespread lesions elsewhere, which are also discoid in character, represent a generalization of the process. The prognosis in such instances usually is milder than that in cases of subacute disseminated lupus erythematosus.

DR FRANCIS E. SENEAR. Dr Brunsting's remarks made me recall a comment made by Dr Hamilton Montgomery several years ago. At that time I presented a patient showing disseminated lesions of lupus erythematosus, these lesions being of the discoid type but somewhat more acutely inflammatory than those observed in the usual case of chronic lupus erythematosus. That patient was definitely ill. She had lost weight, suffered from a moderate degree of prostration and showed mild leukopenia. At that time Dr Finnerud questioned the diagnosis of subacute disseminated lupus erythematosus on the ground that the patient did not present an erythematous type of dermatitis. In reply to this Dr Montgomery stated that at the Mayo Clinic they used the term "disseminated lupus erythematosus" with respect to the degree of systemic involvement which the patient showed rather than with reference to the cutaneous picture. He stated that in patients who presented systemic manifestations of the degree usually encountered in the subacute disseminated type that designation would be used even though the patient presented lesions which were essentially of the discoid rather than of the erythematous type. He also stated that it was the experience of the Mayo Clinic that about 50 per cent of the patients showing systemic involvement of a subacute degree usually succumbed.

I saw the patient to whom I have just referred at school yesterday for the first time in a year or so. She is still an extremely sick person, and I have no doubt but that she will die of her lupus erythematosus, although the eruption is still of the localized discoid type.

DR PAUL O'LEARY, Rochester, Minn. I use the following classification for lupus erythematosus: chronic discoid, localized, generalized, subacute disseminated, acute disseminated, special types, such as bullous and Libman-Sacks syndrome type. The classification is made not only on the clinical features but on the degree of the systemic manifestations as well. Leukopenia and an increased sedimentation rate indicate the degree of systemic involvement, and as the leukopenia becomes greater and the sedimentation rate higher the degree of toxemia is likewise increased. Disproportion in the serum protein-globulin ratios is a result of and not the cause of the systemic reaction. I believe that many of the patients with the subacute form of the disease have minimal cutaneous signs, frequently unrecognizable, although the associated arthralgias and the state of exhaustion may be severe enough to keep the patient confined to bed. A young woman who has arthralgia, fever and leukopenia should be suspected of having the subacute phase of lupus erythematosus, although the cutaneous signs alone do not permit such a diagnosis.

#### Lupus Erythematosus Presented by DR IRENE NEUHAUSER

C. T., a woman aged 42, noticed red patches on the sides of her neck about five months ago. She thought that they were due to irritation from a starched collar, but the patches persisted and have progressed slightly. She is conscious of some sensitivity in this area, but there are no other subjective symptoms. No medication or cosmetics were applied to this area before or after the disease developed.

Examination reveals hyperpigmented atrophic patches of irregular configuration on each side of the neck, extending from the subauricular region to the clavicle. There are telangiectasia, some prominent follicles and a few scanty adherent scales in this area.

The urine was normal. The blood counts were: erythrocytes, 4,360,000, and leukocytes, 6,700, with a differential count of 61 per cent neutrophils, 22 per cent small lymphocytes, 6 per cent large lymphocytes, 8 per cent monocytes, 3 per cent eosinophils and 1 per cent basophils. The hemoglobin content was 82 per cent.

A histologic section taken from the neck showed a thin non-nucleated scale and a flat atrophic epidermis with a continuous granular layer and liquefaction of the basal layer. In the upper part of the corium there was a densely packed infiltrate of lymphocytes, histiocytes and many chromatophores, which extended almost to the epidermis. Narrow mantles of the infiltrating cells extended a little more deeply about some of the blood vessels. The Weigert stain showed the elastic fibers to be thinned and fragmented in the infiltrated areas.

#### DISCUSSION

DR FRANCIS W. LYNCH, St. Paul, Minn. Since the lesions are not characteristic of lupus erythematosus, I am forced to disagree with that diagnosis, although I have no definite diagnosis to offer in its place. The histologic section suggests that the patient might have lichen planus, but the eruption has slight resemblance to that disease.

DR LOUIS H. WINER, Minneapolis. I agree with Dr. Lynch that the histologic section suggests lichen planus with atrophy.

DR MARCUS R. CARO. I thought that histologically a better argument could be made for lupus erythematosus than for lichen planus because there were present atrophy of the epidermis and a considerable degree of liquefaction necrosis in the basal layer. The infiltrate contained a number of chromatophores. All these changes are found in lupus erythematosus to a greater extent than in lichen planus.

DR IRENE NEUHAUSER. Another diagnosis suggested was that of poikiloderma of Civatte. According to Dr. Ormsby's textbook, there are stages of poikiloderma of Civatte in which the histologic changes are indistinguishable from those of lupus erythematosus.



**Hairy and Pigmented Nevus** Presented by DR L F WEBER and DR IRENE NEUHAUSER

D S, a woman aged 24, was born with a hairy and pigmented nevus covering a large portion of the medial surface of the left thigh. About three months ago a small mass appeared on the lower portion of the nevus.

Physical examination shows a palm-sized hairy and pigmented nevus on the medial surface of the left thigh. On the surface there is a bluish-reddish tumor, covered with pus, about the size of a walnut. She has discrete and enlarged glands in the left inguinal region.

A histologic section taken from the lesion showed the changes of malignant melanoma.

## DISCUSSION

DR H E MICHELSON, Minneapolis: This case brings out to me clearly the fact that this type of nevus should be excised by a plastic surgeon who knows how to do it. Some one asked me when I thought it should be done. There is no particular time of course, but the surgeons prefer to operate when the child is old enough to cooperate.

**Linear Eruption** Presented by DR A W STILLIANS

H H, a white American youth aged 19, was sent to a sanatorium in New Mexico in February 1944 because of active pulmonary tuberculosis. Within two weeks of his arrival he noticed an eruption on the right forearm, which itched at times. Four months later a red band appeared on the back of the right index finger, causing the nail to split longitudinally and also causing several fissures to appear over the joints. When the patient was seen last December, a brownish red band, 1 cm in width, extended from the base of the nail along the finger and back of the hand to the wrist. The skin appeared normal for several centimeters proximal to this point, but from there to the elbow the dorsal surface of the forearm was covered with a reticular eruption of scaly yellowish pink macules. This patch faded at the elbow, but about 3 cm above it was a band about the same width as that on the hand but much less fully developed and light in color, extending 6 cm. After mild irritation, due to a 2 per cent chrysarobin ointment, the patch on the forearm became circinate, and the band above the elbow almost faded out. On the forearm, the radial border of the oval was about 5 mm in width and elevated, while the ulnar border was flat and ill defined. This is the appearance at the time of presentation, except that there has been an extension of the band on the arm and a small macular eruption in band form has appeared on the right side of the chest near the median line. Recent lesions on the chest and the back are groups of tiny soft flat papules mixed with macules. There is also a faint trace of the macular eruption on the right subscapular region.

The blood counts were normal, and the Wassermann and Kahn reactions were negative. The urine was found normal.

A histologic section taken from the narrow radial border of the lesion on the forearm showed decided edema of the epidermis and the papillary layer of the cutis with great lengthening and in places separation of the basal cells and a considerable infiltrate of round cells about the small blood vessels. At one point parakeratosis was seen, but for the rest of the section the granular layer was present and there were no persistent nuclei in the horny layer.

## DISCUSSION

DR FRANCIS E SENEAR: The only reason I discuss this case is because several men, seeing the eruption, asked whether it might be an example of lichen striatus. As with any of these linear eruptions, I feel that one has to think of lichen striatus as well as of linear lichen planus, linear nevus and linear psoriasis. This man is beyond the age at which lichen striatus is usually seen. Nearly all my patients were children. Secondly, this eruption has been present for two years. In nearly all my cases of lichen striatus the lesions disappeared spontaneously within a few

years to a few months. This patient has more involvement than has been seen in those cases. He has some irregular bands going across the scapula, and he has some going down across the chest. On the thumb he has a linear patch, and this broadens to form a ring. That ring is a reaction to the use of chrysarobin ointment in this area. Dr Stillians said that there was a patch of dermatitis. I can see nothing in the clinical picture to suggest psoriasis or lichen planus. Without a histologic examination it would be my feeling that it would be a nevus that developed late in life. I do not think that this eruption is lichen striatus.

DR A W STILLIANS. Nevus was ruled out by the fact that there was definite regression in part of the lesion during the period of observation. I consider the eruption a peculiar example of lichen striatus.

**Fixed Eruption Due to a Drug (Sulfathiazole)** Presented by DR M S KAGEN (by invitation)

V B, a man aged 60, entered the hospital on Dec 11, 1944 for treatment of hypertrophy of the prostate gland. From December 18 on, he was given sulfathiazole, 15 grains (0.97 Gm) four times a day. After one week of this medication there developed over the face a diffuse redness, which was accompanied with severe smarting sensations. The medication was discontinued, and after a short time the redness and the discomfort subsided almost entirely. He was again given sulfathiazole in a single dose of 15 grains, and the following morning the redness and the discomfort appeared in the same location. Again the drug was discontinued, and the eruption subsided. He was given the same drug last night, with recurrence of the eruption and the discomfort.

DISCUSSION

There was no discussion of this case.

**Sickle Cell Ulcers Treated with Red Blood Cells** Presented by DR MICHAEL EBERT and (by invitation) DR M S KAGEN

G H, a Negro man aged 21, had an ulcer on the medial aspect of the left ankle two years ago, followed by a similar ulcer on the medial aspect of the right ankle. When the patient entered the hospital two months ago, the ulcer on the left ankle measured  $2\frac{1}{2}$  by  $3\frac{1}{2}$  inches (6.4 by 8.9 cm) and was raised about a quarter of an inch (0.6 cm) above the level of the skin. Ointment of scarlet red U S P and rest in bed were tried for three weeks, with only slight improvement. Moist red blood cells were applied to the ulcers every morning thereafter, moderate pressure being applied. The ulcers have completely healed for the first time.

The blood count showed 4,200,000 erythrocytes and 7,000 leukocytes. The hemoglobin content was 82 per cent. The urine was normal. The Kahn test was negative.

A moist preparation of the blood showed sickling.

DISCUSSION

There was no discussion of this case.

**Granuloma Inguinale** Presented by DR MICHAEL EBERT and (by invitation) DR M S KAGEN

O N, a Negro man aged 44, had an ulcer on the left inguinal area fifteen years ago, which did not increase to more than coin size for five years. During the past ten years the ulceration has extended to the buttocks and about the anus. In 1938 the Kahn test was positive, and for two years thereafter the patient was given antisyphilitic therapy. He has lost considerable weight.

The Frei test elicited no reaction. The Kahn test of the blood was negative. The urine was normal. A smear from the granulation tissue stained with Wright's stain showed Leishmania bodies.

## DISCUSSION

DR THEODORE CORNBLEET Every once in a while a paper on a new treatment or a revived old treatment of granuloma inguinale appears which stimulates dermatologists toward following the author's recommendations in the treatment of their patients. The results have been poor enough to make me pessimistic. For a while Fuadin seemed to improve the outlook, but it too has not stood the test of time. In some patients there was a temporary improvement with this substance, after which there was a relapse. Resin of podophyllum was irritating and did not do the patients any good. Surgical intervention would seem to offer more when it is feasible. About four or five years ago I sterilized antimony solutions by passing them through a Berkefeld filter. These were no more efficacious than those prepared by heating.

**Ainhum** Presented by DR THEODORE CORNBLEET

A Negro man aged 47 was born and reared in Louisiana. He has lived in Illinois for twenty years. The left small toe was spontaneously amputated five years ago. The right small toe has been undergoing the present process for two years.

## DISCUSSION

There was no discussion of this case.

**Neurotic Excoriations** Presented by DR DAVID V OMENS, DR HAROLD D OMENS and (by invitation) DR M S KAGEN

S B, a white girl aged 18, was admitted to the hospital because of an eruption involving the face, the chest and the back and consisting of small bullae and crusts of variable size and configuration but compatible with pemphigus erythematosis. However, histologic examinations of sections on two occasions failed to reveal any pathologic changes.

This girl has congenital syphilis and has had considerable treatment, beginning at the age of 5 years and continuing for about five years.

The urine and the blood count were normal. The Wassermann and Kahn tests were negative. The basal metabolic rate was — 6 per cent.

The patient complains of attacks of diarrhea and periodical attacks of palpitation. She suffers from sleeplessness and anxiety, and the pulse rate is rarely under 100 beats per minute.

## CLEVELAND DERMATOLOGICAL SOCIETY

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Feb 22, 1945

**Lichen Sclerosus et Atrophicus** Presented by DR W R HUBLER

A W, a white girl aged 11 years, has had slightly pruritic white spots on the forearms, the shoulders and the feet since May 1944. They appeared suddenly as flat white papules. At no time were they raised or violaceous. There has been no recent change in the eruption.

There are numerous depressed atrophic white areas on the flexor surfaces of the left forearm and the flexor and the extensor surfaces of the right forearm. A few similar areas are present on the shoulders and the trunk. The legs and the dorsa of the feet are also involved. The areas are distributed in a guttate and linear fashion. Many of the lesions have coalesced without losing the outlines of the original papules. Black comedo-like plugs are present in the midportions of most

of the guttate atrophic papules. The vulva, the mouth and the scalp are free of lesions.

The hemogram was normal except for slight hypochromic anemia, the blood sugar level was within normal limits. The Wassermann and Kahn reactions of the blood were negative.

#### Lichen Sclerosus et Atrophicus Presented by DR CLYDE L CUMMER

Mrs T F, a white woman aged 55, was seen at St Vincent's Charity Hospital on June 7 1944 with an eruption which she said had been present for one year.

On the flexor surfaces of the wrists are plaques about the size of a silver dollar, showing thickening of the skin. The surfaces are smooth and shining. The color is that of an oyster shell. At the periphery there is a slight blue coloration. Comedo-like plugs and multiple pinpoint depressions are seen. Atrophy is present. In the other regions the lesions are smaller, those in the crural areas being a few millimeters in diameter only while those on the dorsa of the hands vary from this size to about 1 cm. They also show bluish borders.

The histologic examination was made by Dr W P Jennings and reported as follows: "The section consisted of a portion of skin containing a circumscribed lesion. The lesion was characterized by atrophy of the papillae, increase and condensation of the fibrous tissue in the dermis and almost complete loss of elastic tissue. There was increased vascularization with peripheral cuffing. The vascular reaction was made up of numerous lymphocytes and some fibroblasts. The reaction occurred chiefly at the periphery of the lesion. In the uninvolved portions of the skin, the collagen was loosely arranged and edematous."

After twelve intramuscular injections of bismuth subsalicylate in oil at weekly intervals, there seemed to be some involution with atrophy around the edges of the lesions.

#### DISCUSSION OF THE TWO PRECEDING CASES

DR JAMES R DRIVER: The lesions of A W were appearing in scratch marks on the extremities.

DR CLYDE L CUMMER: I presented a case of lichen sclerosus et atrophicus before this society on March 25, 1943 (*ARCH DERMAT & SYPH* 49 449 [June] 1944). The eruption had been present for five years or longer. The patient was given two courses of bismuth subsalicylate in oil intramuscularly. When the patient was seen for another complaint on Feb 16, 1945, it was found that the lesions of lichen sclerosus et atrophicus had disappeared completely.

#### A Case for Diagnosis (Lupus Vulgaris?) Presented by DR CLYDE L CUMMER and DR C G LAROCO

R M, a Negro aged 38, was referred to the outpatient department of St Vincent's Charity Hospital for further treatment. The patient is indefinite as to the length of time "sores" have been present on his body—maybe for several years. He has latent syphilis, for which he received continuous treatment for two years ending March 1944. Since then he has had injections of a bismuth compound in oil at intervals.

On the upper lip and around the nares, at the angles of the jaw and over the penis and the scrotum are pinhead-sized nodules. On the upper lip there is circular grouping around a scar. There is scarring with loss of tissue on the septal side of the left naris. There is no clinical evidence of tuberculosis of the lungs or other tissues.

The Wassermann and Kline reactions of the blood were strongly positive. The hemogram and the urinalysis revealed normal conditions. A roentgenologic examination of the chest showed intensification of the hilar shadows with what probably was a single, slightly enlarged uncalcified node in the left hilus. An examination of the hands and fingers and the feet and toes showed a single punched-out zone of rarefaction in the head of the proximal phalanx of the right fifth toe. A histologic

study revealed that the subcutaneous tissue contained numerous noncaseating tubercloid lesions. The changes are consistent with tuberculosis or possibly sarcoidosis.

### **Lupus Vulgaris** Presented by DR. W. R. HUBLER

Mrs. N. Y., a white woman aged 49, first noticed a small red area "like a little red berry," on each thigh in 1905, when she emigrated from Europe. These have increased slowly in size since then. Following eight roentgen ray treatments, two years ago, ulceration appeared on the right thigh. There has been no other treatment.

An oval, well demarcated red scaly granulomatous plaque, 5 by 7.5 cm., is seen on the anterior portion of each thigh. The middle portions have patchy depigmentation and atrophy. Telangiectasia extends from the centers to beyond the borders of the plaques in some areas. The plaques are raised and red and show deeper soft brownish red macules, 0.5 cm. in size. The remainder of the physical examination revealed no abnormalities.

The hemoglobin content was 13 Gm., and the leukocyte count was 7,100. The blood sugar was within normal limits. The Wassermann and Kahn tests of the blood were negative. An intradermal injection of old tuberculin diluted 1:10,000 gave an indurated papule, 1 cm. in size. A roentgenogram showed that the chest was normal. Biopsy of two plaques revealed essentially the same changes. There were moderate parakeratosis and hyperkeratosis, irregular acanthosis, with intercellular and intracellular edema, and liquefaction degeneration of the basal layer. The entire corium was edematous and contained dilated capillaries. Numerous large nests of epithelioid and lymphocytic cells filled most of the upper two thirds of the dermis surrounding the dermal appendages. They were accompanied with numerous partially formed and complete foreign body and Langerhans' giant cells. A small amount of coagulation necrosis was present in a few of the nodules. In the background the connective tissue was displaced from the nodules and appeared only as thin fibrillar strands between them. No acid-fast bacilli were seen with Ziehl-Neelsen stains.

A salt-free diet was prescribed and has been used by the patient since Dec. 20, 1944. Considerable involution of the plaques can be seen. They are less indurated, slightly smaller and of a lighter color. The apple jelly nodules are probably more apparent because of this.

### DISCUSSION OF THE TWO PRECEDING CASES

DR. CLYDE L. CUMMER: When Dr. LaRocco and I first saw R. M., we were in doubt as to whether we were dealing with lupus erythematosus or tuberculosis of the skin on account of the infiltration. The appearance was that of Leloir's erythematoid lupus vulgaris. We found a nodule with apple-jelly-like appearance, which was removed for biopsy. It showed the histologic changes associated with tuberculosis. I am satisfied to call this eruption tuberculosis of the skin.

### **Sarcoidosis** Presented by DR. E. W. NETHERTON

Mrs. M. E., a white woman aged 35, has had brownish purple papules and plaques on the arms and the shoulders since 1941. These have gradually increased in size and number. The cutaneous eruptions were not accompanied with subjective symptoms. The patient's chief complaints were lack of endurance, headache, pain in the chest and a cutaneous eruption which had been present for three years. During this time she felt listless but had had no acute illness. Her tonsils were removed in March 1943, and in September her spleen was removed. An examination of the spleen showed extensive involvement of a sarcoid nature. The Mantoux test done on two previous occasions elicited no significant reaction. Previous roentgenograms showed a normal chest.

There are several brownish red smooth flat doughy epidermal and dermal nodules scattered over the arms and the trunk. There is one small pea-sized

nodule on the right cheek. The nodules vary in size from that of a small lima bean to that of a twenty-five cent piece.

The hemogram showed mild secondary anemia. The Wassermann and Kahn reactions of the blood were negative. A roentgenogram made on Feb 17, 1945 showed the heart to be normal. There was decided fibrosis in the lower lobe of the right lung, with fibrous infiltration of the upper lobe and the apex. There was a little fibrosis in the lower lobe of the left lung. This was interpreted as pulmonary tuberculosis involving the right apex. Biopsy showed that the epidermis was slightly thinner than normal. The papillary layer of the epidermis was uninvolved. The subpapillary and upper portions of the corium contained numerous circular and fusiform irregular masses, composed principally of large epithelioid cells and surrounded by a narrow dense zone of fibrous connective tissue. There were numerous giant cells of the Langerhans type. There was a small amount of lymphocytic infiltration at the periphery of some of the foci. There were no areas of necrosis.

#### Sarcoidosis with Ulceration Presented by DR W R HUBLER

Mrs S W, a white woman aged 37, noted a plaquelike lesion on her right leg five years ago. It was excised. The histologic diagnosis was foreign body reaction. New lesions recurred in the scar and on the adjacent thigh. These crusted at times and often partially disappeared, leaving little scar formation. However, she has not been free of lesions at any time. She has received eleven roentgen ray treatments to the right thigh, with little benefit. Ointments, "iron and arsenic" injections and vitamin A were prescribed, without benefit. She has had psoriasis for twenty years.

On her first visit to the clinic, on May 1, 1944, three granulomatous scarred plaques were present on the anterior part of the right thigh, and faint, light brown plaques, the size of a 25 cent piece, consisting of coalesced glossy pinhead-sized papules, were present on the left shoulder. Since that time, recurrent ulcers have developed on the plaques on the right thigh. These ulcers have been excised, with healing, but eventual recurrence is the rule. In addition, many new lesions have appeared on the body. Recently, the ulcerated areas on the right leg have become painful.

There are three large indurated red-brown plaques on the anterior portions of the right thigh. These present numerous glass pinhead-sized, light red-brown papules along portions of their periphery. On the largest plaque is an irregular ulcer, 5 by 10 cm, with a purulent base. An ulcer, 2 by 3 cm, is present on the medial plaque. Another plaque shows sparse heavy adherent crusting. Numerous sharply demarcated round reddish brown granulomatous plaques, varying from 2 to 6 cm in diameter, are scattered over the trunk, the neck and the arms. The outlines of the constituent glass pinhead-sized papules are preserved on the smaller lesions. A large lesion on the right side of the trunk is covered with a heavy black crust. There are a few smaller lesions on the vulva. A few circinate lesions of psoriasis are present on the trunk, the scalp and the right elbow.

Repeated hemograms have revealed slight hypochromic anemia. The urine and the blood sugar level were normal. The Wassermann and Kahn reactions of the blood were negative. The tuberculin test, with a 1:10,000 dilution of old tuberculin, resulted in the appearance of an indurated papule, 2 cm in size. Roentgenograms revealed that the chest and the hands were normal.

The histologic examination of a nonulcerating portion of a plaque on the right leg revealed patchy parakeratosis and irregular acanthosis. Scattered profusely throughout the lower two thirds of the cutis were numerous large mononuclear cells, lymphocytes and eosinophilic leukocytes. Many large multinucleated giant cells of the Langerhans type were scattered throughout the cutis. No acid-fast bacilli were identified with the Ziehl-Neelsen stain. In the deeper portions of the dermis and the subcutaneous tissue there were similar cells, along with circular groups of epithelioid and giant cells around the blood vessels.

Rest, sunlight, supplementary fat-soluble vitamins, neoarsphenamine and injections of solution of sodium arsenate have been prescribed, all without benefit. She also received 1,000,000 units of penicillin, this course of treatment was followed by a severe urticarial eruption lasting from ten to twelve days. Penicillin therapy and a salt-free diet were of no benefit.

#### **Sarcoidosis** Presented by DR E W NETHERTON

J M, a man aged 46, came to the Cleveland Clinic on Feb 1, 1945. His family and past histories were unimportant. His complaint was "lumps" in the skin of the upper extensor surfaces of the arms. These lesions appeared for the first time in 1940. They were small at first but gradually enlarged. New lesions appeared from time to time until, at this examination, the upper lateral and extensor surfaces of the arms, the buttocks and the lower portion of the back were involved. There were no subjective symptoms. The patient's general health has always been good.

There are dull red to reddish brown smooth doughy cutaneous and subcutaneous nodules, ranging in size from that of a hazelnut to that of a small English walnut, on the lateral surfaces of the arms, in the deltoid region and over the upper portion of the back, the lower portion of the back and the sides of the trunk. There are a few lesions on the buttocks. The lesions are poorly defined and not tender. There has been no tendency of the lesions to ulcerate. The larger lesions are covered with small dry adherent scales.

The hemogram showed normal conditions. The Wassermann and Kahn reactions of the blood were negative. An intradermal injection of 0.1 cc of 1:1,000 old tuberculin evoked no significant reaction, but a strongly positive reaction was elicited with old tuberculin diluted 1:100.

A roentgenogram of the chest showed extensive fibrosis, particularly in the midlung field. The apexes and the peripheral regions of the lungs are normal. There are a few early calcifications at the upper part of the right hilus and in the midportions of the lungs. A roentgenogram of the hands showed hypertrophic arthritis of the finger joints, particularly severe in the distal joint of the thumb. There is no evidence of rarefaction of the phalanges. The roentgenograms were finally interpreted as evidence of an extensive old bronchitis and hypertrophic arthritis of the hands.

Biopsy of a medium-sized nodule was performed. The histologic section showed slight thinning of the epidermis and slight hyperkeratosis, with slight lymphocytic infiltration of the papillary layer of the corium. Deeper in the corium there were numerous circular irregular granulomatous masses, composed of epithelioid cells, with a rich peripheral infiltration of lymphocytes. There was an occasional giant cell of the Langerhans type but no foci of necrosis.

#### **Sarcoidosis** Presented by DR E W NETHERTON

Mr F B, a railroad fireman aged 35, came to the Cleveland Clinic on Feb 25, 1943. He complained that the superficial axillary and inguinal lymph nodes had been enlarged for about eighteen months. He had no other complaints, and his general health had been good. His family and past histories were unimportant. Examination showed discrete firm enlarged lymph nodes in the axillary and cervical regions. The epitrochlear nodes were palpable. The spleen was not palpable. The liver was felt on deep inspiration. There were no cutaneous lesions at this time. A provisional clinical diagnosis of Hodgkin's disease was made. Histologic examination of a lymph node removed from the cervical region showed changes consistent with the diagnosis of sarcoidosis.

The patient was again seen on Dec 15, 1944, because of cutaneous lesions on the forehead, the scalp and the elbows. These lesions have been present for about two years. They consist of oval and round, sharply demarcated, yellowish brown, slightly scaly, infiltrated plaques on the forehead and the scalp, near the hair line of the forehead. The lesions on the forehead are similar to those on the scalp but

differ in that they show atrophy of their central portions. There are split pea-sized pink infiltrated smooth papules on the elbows.

The hemogram revealed no abnormalities. The Wassermann and Kahn reactions of the blood were negative. The Mantoux test showed no reaction to a 1:100 dilution of old tuberculin. A roentgenogram of the chest showed bronchovascular markings, which were unusually prominent throughout the lungs. Scattered along the bronchovascular trunks of the left lobe were several nodules, the largest of which measured 5 cm. in diameter. There was considerable peribronchial infiltration in the lower part of the right lung. The mediastinal lymph nodes were enlarged.

The histologic examination of a small papule removed from the right elbow showed the following conditions. The epidermis was covered with a layer of hyperkeratosis. The granular layer was thickened, and the rete mucosum was thin. There were numerous sharply demarcated nodules composed of epithelioid cells. There were a few giant cells of the Langerhans type in the upper and middle portions of the corium. These nodules were surrounded by narrow zones of collagenous fibers. There were no areas of central necrosis. A few of the foci of infiltration were surrounded by slight amounts of lymphocytic infiltration.

The changes observed in the older lesions of the forehead were somewhat similar. However, the epidermis was thin and was invaded by the cells infiltrating the upper portion of the corium. The infiltration consisted of less well defined single, but more often coalescent, tubercle-like foci of infiltration, consisting of epithelioid giant cells and a moderate number of mononuclear cells, chiefly small lymphocytes. There were some small areas of focal necrosis. No acid-fast bacilli were seen in the Ziehl-Neelsen preparation.

#### DISCUSSION OF THE FOUR PRECEDING CASES

DR HAROLD N. COLE. In regard to M. E., I thought that the eruption was a typical example of sarcoidosis with apple-jelly-like nodules which clear in the centers.

DR W. R. HUBLER. S. W. was presented because of the unusual combination of lesions. The ulcerated areas of sarcoid on the thigh and the tumor-like plaques on the side of the trunk appeared suddenly. The lesions on the legs are of several years' duration. The ulcers appeared about six months ago and have been excised several times. Healing was by secondary intention each time, which was facilitated by penicillin ointment applied locally. It was because of the local infection that 1,000,000 units of penicillin was given intramuscularly over a period of seven days. Each ulcer that was excised and completely healed has recurred in the same area. All the specimens have shown a histologic picture compatible with sarcoid or atypical erythema induratum. Numerous eosinophils have been found in the more recent section. The histologic appearances revealed on biopsy of the tumor-like plaque on the right side of the trunk were identical with those observed in the other biopsies and were not compatible with mycosis fungoides. A lepromin test was positive.

DR E. W. NATHLINTON. S. W. was presented before this society several years ago as having sarcoidosis, but the diagnosis was not accepted. Since she has been under observation the lesions have become disseminated over the body rapidly within the last few months. It is interesting to point out that this patient has a positive reaction to tuberculin in the dilution of 1:10,000.

DR HAROLD N. COLE. In regard to the cutaneous disease of S. W., clinically the diagnosis should be mycosis fungoides in the fungating stage. The microscopic picture was characteristic of sarcoidosis but I would recommend further study. The patient's clinical appearance is certainly not typical of sarcoidosis.

It is unusual to see so much scaling as in the case of J. M., the man with the lesions on his arm. I would not be able to make a clinical diagnosis. It would be necessary to have a biopsy performed. The patient did not have any changes in his fingers.



DR E W NETHERTON With reference to J M, Dr Cole mentioned that a clinical diagnosis could hardly be made. However, the histologic sections of the specimen removed for biopsy show the typical changes of sarcoid. The man had a negative reaction to old tuberculin in a 1:1,000 dilution.

#### **Amyloidosis of Skin** Presented by DR JAMES H BARR JR

A M, a white man aged 59, was admitted to the dermatologic outpatient department of University Hospitals on Dec 13, 1944. At that time he complained of an intensely pruritic eruption of one year's duration on the extensor surfaces of both legs and the left forearm. This eruption first appeared in small groups of lesions above the ankles. The lesions gradually increased in number and extent. The patient has remained in good health throughout this period. The diagnosis of lichen planus was made of a previous cutaneous disease observed at Cleveland City Hospital in 1934.

The general physical examination, including laryngoscopic examination, revealed normal conditions except for the skin and a blood pressure of 175 systolic and 90 diastolic. There are numerous discrete firm hemispheric, seemingly translucent, light brown papules, topped with a hemorrhagic crust, symmetrically located on the extensor surfaces of the lower legs. A tendency toward grouping can be discerned. Similar lesions are manifest on the left wrist.

The hemogram was of interest in that there were 20 per cent normal mature monocytes in the differential count. The results of a complete urinalysis were normal. The result of the Kline exclusion test, the amount of blood urea nitrogen and of plasma proteins, the albumin-globulin ratio, the serum cholesterol level and the blood urea clearances were well within the ranges of normal. A roentgenologic examination showed that the chest was normal. On histologic examination, sections stained with crystal violet showed a hyaline material in the upper part of the dermis, having the staining property of amyloid.

Calamine liniment, containing 0.5 per cent menthol and 10 per cent solution of coal tar, has been prescribed, with satisfactory relief of the pruritus.

#### DISCUSSION

DR E W NETHERTON I am sure that Dr Driver will remember a case that I presented before the society many years ago, as one of a shin guard type of lichen planus. In all probability, it was also a case of amyloidosis, as it resembled the clinical features of the case presented today. The sections showed characteristic amyloid changes.

DR JAMES R DRIVER From the standpoint of therapy I recall a case in which occlusive dressings were used, which kept the patient from scratching. Over a period of a few months the eruption regressed completely.

DR RUBEN DAVID AZULAY, Rio de Janeiro, Brazil (by invitation) I should like to ask which treatment is regarded as most effective. I can mention one experience I had with the congo red test. The lesions cleared so satisfactorily that the congo red test has been used as therapy in my country.

DR CHARLES G LAROCO In reply to Dr Azulay, I recall a case of amyloidosis in which the result of the congo red test was positive for this disease, but subsequent follow-up showed no benefit from the congo red dye.

#### **Pustular Psoriasis, Pustular Bacterid?** Presented by DR E W NETHERTON

Mr J O, a clerk aged 31, is presented because of an eruption of one and a half years' duration. The family history is unimportant. His right hand had been amputated because of an accident. The eruption first appeared as a group of "blisters and pustules" on the thenar eminence of the left palm. Six months later, similar lesions developed on the left foot and the inner surface of the left heel. The eruption spread gradually to involve the insteps, the adjacent portions of the soles and the large toes, and more recently lesions have appeared on the

pretibial regions, the knees, the left forearm and the chest. Itching has been present but not troublesome. The eruption failed to respond to roentgen ray therapy and various topical remedies.

There are large well defined red irregular plaques, involving the insteps, the soles, the inner surfaces of the heels and the left palm and wrist. The surfaces of the lesions are in places covered with large gray adherent scales. In other areas there are numerous pinhead-sized tense pustules, while in still other areas the surface of the plaques has a fine granular appearance. There are various-sized erythematous scaly plaques of the psoriasiform type on the extensor surfaces of the legs, the midportion of the chest, the forearms and the knees. The scalp is not involved. The large toe nails are rough, thickened and friable, and the nail fold is involved by a scaly erythematous eruption, similar to that involving the instep.

The hemogram was normal. The Wassermann and Kahn reactions of the blood were negative. Material removed from the thickened nails and from the hands and the soles for potassium hydroxide preparation did not reveal hyphae.

A histologic study of tissue removed from a psoriasiform lesion of the lower portion of the right leg showed a change which involved chiefly the epidermis. The surface of the epidermis was covered with a layer of hyperkeratosis and parakeratosis. There was acanthosis. The papillae varied in length and width, and some were covered with a thin layer of epidermis. The basal cell layer was intact. There were edema, vascular dilatation and moderate perivascular lymphocytic infiltration in the papillae and the subpapillary portion of the corium. There was no typical Monro abscess. However, there were small collections of leukocytes in some of the hyperkeratotic and parakeratotic scales.

#### DISCUSSION

DR HAROLD N COLE All dermatologists see recalcitrant pustular eruptions of the palms and the soles. It is rare to see one for which the term "pustular psoriasis" may be used. The patient has typical pustular areas on the palms and the soles, along with lesions over the sternum, that are suggestive of a psoriatic process.

DR E W NETHERTON Dr Cole has mentioned the main reason for showing this patient. All the members have seen chronic scaly pustular erythematous lesions on the palms and the soles such as this patient presented, and have had considerable difficulty in arriving at the proper diagnosis, the diagnosis often resting between bacterid and pustular psoriasis. In this case, however, there are definite, rather typical lesions of psoriasis on the knees and the legs. The histologic study of biopsy material shows changes characteristic of psoriasis.

#### Trophic Ulcers Following Nerve Resection Presented by DR CLYDE L CUMMER

M J F, a white man aged 63, was operated on in February 1932 for tic douloureux of the left side of the face, presumably a resection of the gasserian ganglion was done. He had no difficulty with the skin of the left side of the face and the scalp for almost ten years, although there was complete loss of sensation in this area. There were trophic ulcers of the cornea of the left eye. This resulted in scarring and impairment in vision.

On Sept 7, 1944 he presented deep irregular scars on the left side of the face. On the upper left eyelid was a clean sluggish deep ulcer, almost covering the entire lid. There was a similar ulcer on the left side of the forehead and numerous areas resembling excoriations on the left vertex.

Ointment of scarlet red N F was prescribed, with great improvement in the ulcers of the skin.

#### DISCUSSION

DR HAROLD N COLE The patient gives a typical history of neurotic excoriations. Granted, there is an area of trophic change, but, in addition, he has been picking the areas.

## Book Reviews

**Skin Diseases in Children** By George M MacKee, M D, and Anthony C Cipollaro, M D Second edition Price, \$7 50 Pp 448, with 225 black and white photos New York Paul B Hoeber, Inc (Medical Book Department of Harper & Brothers), 1946

This excellent book in its second edition has been greatly enlarged and completely rewritten It contains twenty-two chapters, including four new ones on dermatologic allergy, the exanthemas, congenital anomalies and congenital syphilis by other writers No attempt at scientific classification has been made, the subjects being discussed partly on etiologic and partly on pathologic grounds and partly on the basis of clinical similarity

The book is written mainly for the general practitioner, though much information of value to the dermatologist is given Most of the treatment suggested is based on the wide experience of the authors An adequate bibliography is included at the end of each chapter

One of the most valuable features of the book is the two hundred and twenty-five black and white clinical photographs They are unusually good, well chosen and, owing to the fairly heavy glazed paper used in the entire book, splendidly reproduced The frontispiece, consisting of four colored pictures, does not compare in value with the black and white illustrations

The authors have carefully followed the Standard Nomenclature of Disease, though in 2 instances slips were made, one being the use of "lymphogranuloma inguinale" in place of "venereal lymphogranuloma," and the other, a minor but common mistake, "nevus unius lateralis" instead of "nevus unius lateris"

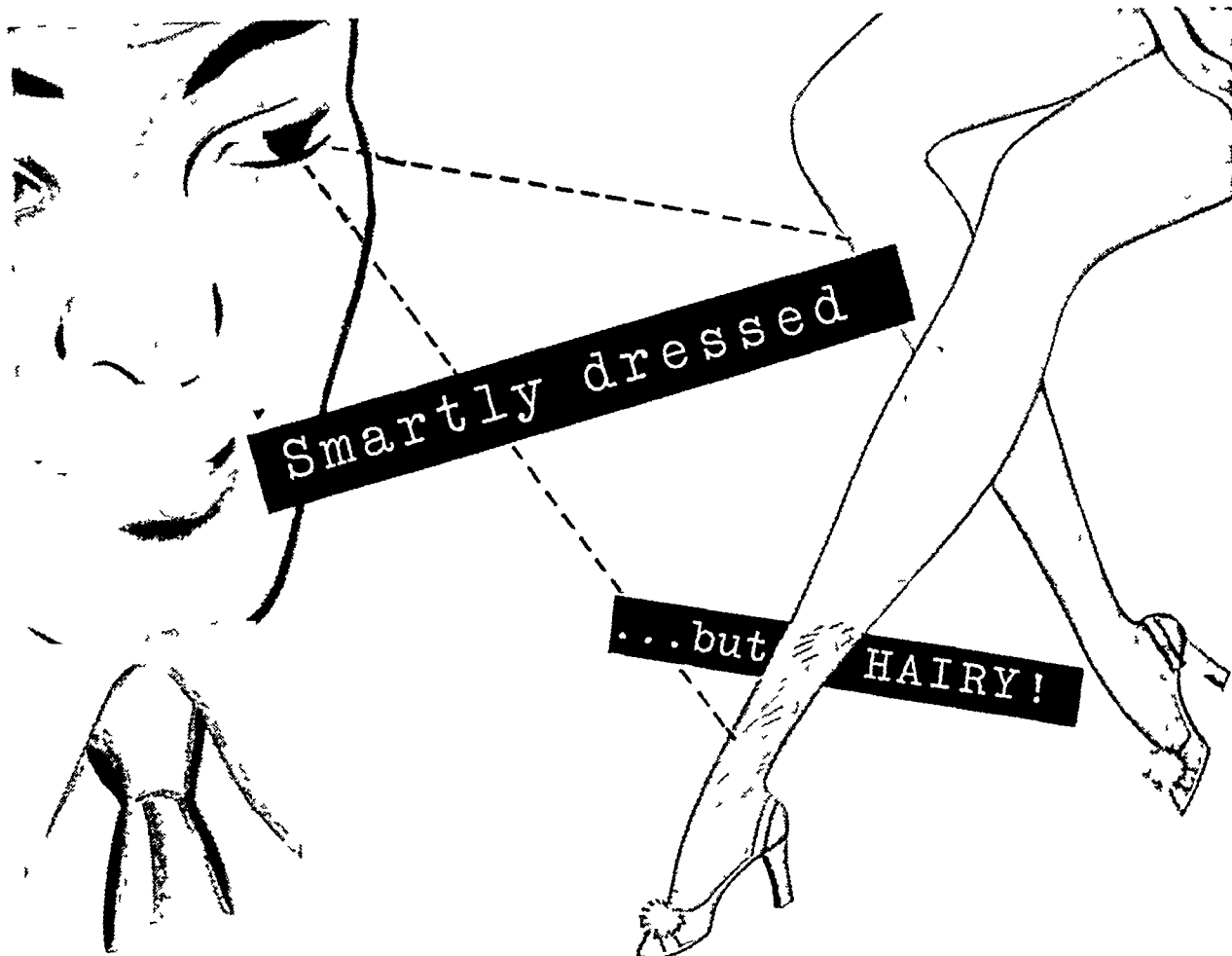
The book is clearly written and contains up-to-date information which makes it a most valuable treatise for the dermatologist and general practitioner alike

**Corky the Killer A Story of Syphilis** By Harry A Wilmer, M D Introduction by Paul A O'Leary, M D, with forewords by Joseph E Moore, M D and by Kendall Emerson, M D Price, \$1 Pp 66 New York American Social Hygiene Association, Inc, 1945

The author has told the story of syphilis to the layman in a most interesting and graphic manner The villain in the story, called Corky, represents a spiral-shaped *Treponema pallidum*, who with his millions of comrades attempts to destroy every part of the human body The illustrations by the author are unique and graphically show the attacks of the spirochete on various organs Each page gives the story of Corky's machinations in understandable language At the bottom of each page the scientific facts are explained in language any layman can understand A book that is limited to the scientific story would not be read by as many laymen as one that is combined with the bizarre drawings of Corky and his experiences This book should have a large sale and is a distinct contribution to the fight against syphilis

## News and Comment

**Section on Dermatology and Syphilology, American Medical Association, Centennial Anniversary Meeting**—All who desire to read papers before the Section on Dermatology and Syphilology at the Centennial Anniversary meeting of the American Medical Association in Atlantic City, N J, in June 1947 will please write to the Secretary There will be fewer positions available for members on account of invitations to a few foreign guest speakers Applications should be addressed to Clinton W Lane, M D, Secretary of the Section on Dermatology and Syphilology, Metropolitan Building, St Louis 3, Mo



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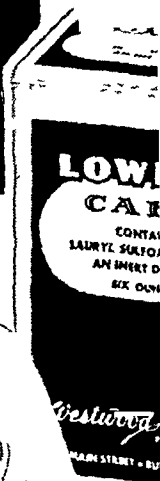
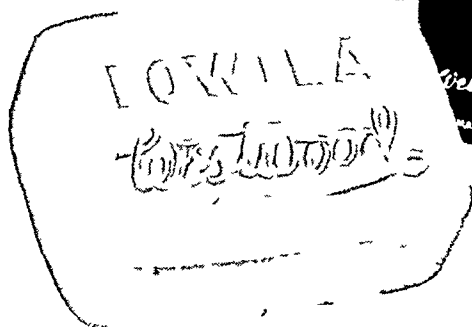
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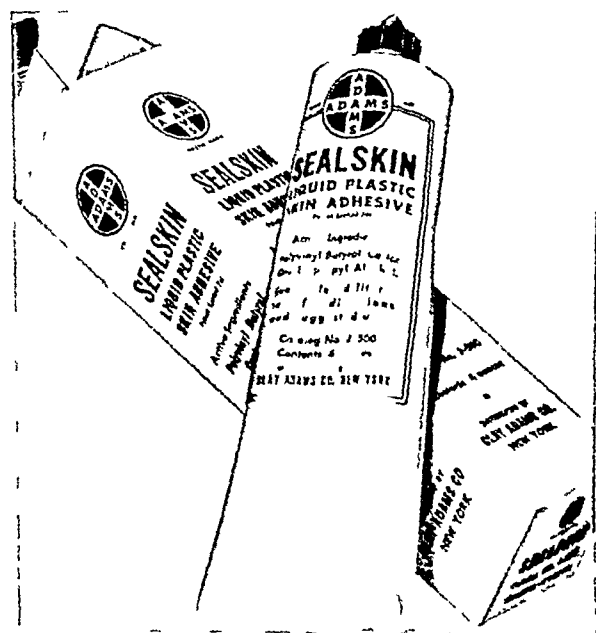
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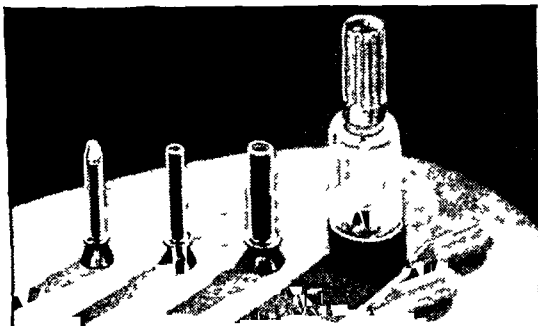
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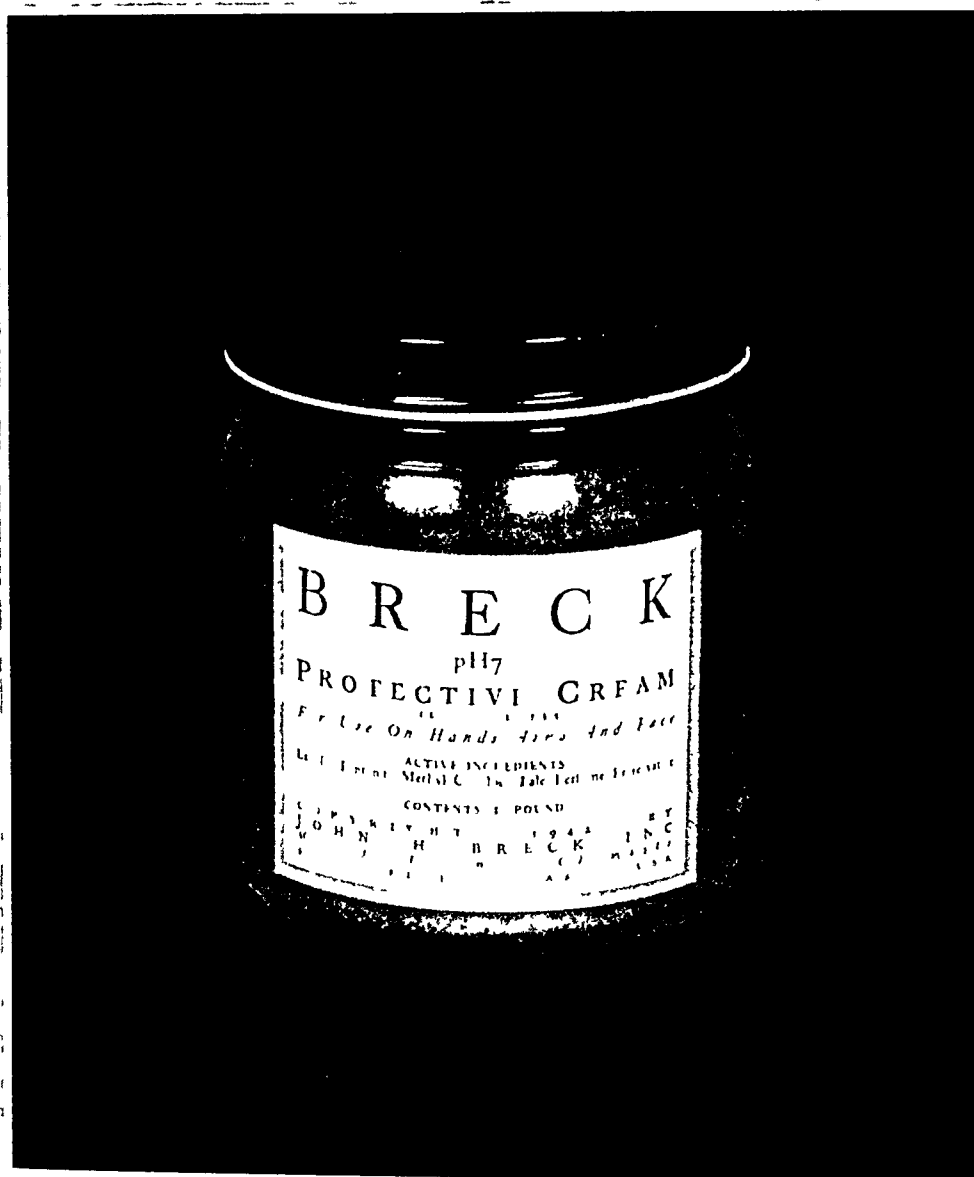
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<sup>1</sup> I. H. Blank, *Arch. of Derm. and Syph.* 39: 811-824 (1939).  
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